

## 82- SUBMISSIONS FACING SHEET

			MICROFICE	IE CONTROL LA	BEL	
			L			
REGISTRANT'S	NAME _	Antiens	e The	capentres	Limite	d
*CURRENT ADD	RESS	Leve!	1		· · · · · · · · · · · · · · · · · · ·	- CRESTO
	. 1	0. Wal	lace &	Ivenue	PRIL	
	7	Toorak	· Vic	taria	NON	73 2004
4.		3142	Hust	alla	TH	OMISON
**FORMER NAM	Σ				FI	NANCIAL
						•
**NEW ADDRES	s _		···	,		
			·		-	
	7:100.1		· · · · · · · · · · · · · · · · · · ·	<del></del>		
FILE NO. 82-	3484		FISCAL	YEAR	,-	а · ш ·
				<del></del>		<del></del>
• Complete for	initial submission	es only co Please	note name and a	ddress changes		
מאד	TCATE FORE	1 TYPE TO E	E USED FO	R WORKLOAD	FNTDV.	
			<u> </u>		*****	
		, ··· )				
12 <b>G3</b> -2B (I	NITIAL FI	LING)	AR/S	(ANNUAL RE	PORT)	
12G32BR (R	EINSTATEM.	ENT)	SUPPL	(OTHER)		4
DEF 14A (P	ROXY)					
				· OICF/E	8Y: E	35
						23/04
					11/	4107



ASIC

## RECEIVED

2004 NOV 16 P 12: 18



Australian Securities & Investments Commission

## Change to company details

Form 484 — Corporations Act 2001

## Section A

Section A may be lodged independently if no changes are to be notified via Sections B or C.

- Use this form to notify ASIC of:

A1 Change of address

A2 Change of name - officeholders or members

A3 Change - ultimate holding company

484 B - appoint/cease officeholders, change to special status 484 C - issue/cancel shares, change share structure and members' register

If there is insufficient space in any section of the form, you may photocopy the relevant page(s) and submit as part of this lodgement

## Company details

Company n	ıame					
Por	15505	JE T	HERAF	'Emcs	LIMITER	
ACN/ABN						
<u> </u>	<u> </u>	<u>060</u>	245			

## A1 Change of address

This section allows a new address to be applied to one or more purposes (eg registered office and principal place of business). You may copy and attach another Section A1 for each new address.

## New address

(A PO Box is only allowed for a member address)

## Date of change

For members include date of change to members' register.

Continues on next page...

ASIC Form 484 Section A 1 July 2003

At the office of, C/- (if applicable)	
Office) unit, level, or PO Box number (A PO Box is only	rallowed for a member address)% 2011 11 11 11 11 11 11 11 11 11 11 11 11
Street number and Street name	
27 MUNRO STREET	
Suburb/City HAWTHORN GAST	State/Territory:
Postcode Country (if not Australia)	
3123	
Date	
	Page 1 of 4

## Apply address to (You can apply the new address to one or more of the following — registered office, principal place of business, etc). Registered office address A change to the registered office address takes effect either 7 days after lodgement of the notice or a later date specified in the

notice.

Member'	s add	ress
---------	-------	------

If there are more than 20 members in a share class, only address changes for the top 20 need be notified.

	Registered office address
	If registered office changed, does the company occupy the premises?
	U yes no. > no. > server provide the control of th
	if no, name of occupier
	Occupier's consent (Select box to indicate the statement below is correct)
	The occupier of the premises has consented in writing to the use of the specified address as the address of the registered office of the company and has not
	withdrawn that consent.
	Principal place of business address
$\dot{\theta}$	
: <u>  Y</u>	Company officeholder's residential address  Family name Given names
	DIAMOND   MARK PAUL   Place of birth (town/city) (state/country)
	MELBOURNE, AUSTRALIA Date of birth
	03103164
	D D M M TY Y
	Place of birth (town/city) (state/country)
	Date of birth
:	Member's address
	Family name Given names
	Family name: Given names:
	When a member is a company, not a person  Company name (only if a member)
	ACN/ARBN/ABN Country of incorporation (if not Australia) z.
	Company name (only if a member)
	2
276 B.	

oply change of name to	
ne following person (or entity) has nanged their name (Select one or more oxes)	Director Alternate director  Secretary Member
ersonal name change eg change by deed poll, marriage. To egister a new officeholder go to B1)	Their previous name was (Provide full given names, not initials)  Family name.  Given names
nember's name there are more than 20 members in a hare class, only name changes for the	Place of birth (town/city) (state/country)
p 20 need be notified. ate and place of birth are not required or members.	Date of Birth  DI / DI
	Their new name is (Provide full given names, not initials)  Family name  Given names
	Date of change  [Disc D] [Mr. M] [Y Y]
Organisation name change (member only)	The previous organisation name was
(When a member is a company, not a person, and the company has changed its name)	The new organisation name is  ACN/ARBN/ABN
	Date of change:  Description of the District o
A3 Change — ultimate Use this section if there is a change to	
The change is	There is a new ultimate holding company  Company name
	ACN/ARBN/ABN Country of incorporation (if not Australia) OR OR
	The ultimate holding company has ceased operation as the ultimate holding company Company name
	ACN/ARBN/ABN Country of incorporation (if not Australia)  OR
	The ultimate holding company has changed its name (date of change not required)  New name
	ACN/ ARBN/ ABN Country of incorporation (if not Australia) OR:
	Date of change
ASIC Form 484 Section A 1 July 2003	D D M M M Y Y

## Signature

This form must be signed by a current officeholder of the company.

NATALIÉ	KORCHE	
Capacity 4		
Director		on on the caracter of the late.
Company secretary		
Signature		
N. Korc	rev	
Date signed		
0 9 1 0 7 1 C		

## Lodging party details

Please notify the registered agent details (if applicable) and to whom queries about this form should be directed.

## **Registered Agent details**

If this form is being lodged by an ASIC registered agent, please complete agent name and number

## Queries about this form

You can nominate an officeholder, lodging party or ASIC registered agent

			J.,,;;;;;;
IC registered agent nu	moer		7-1-7-12-717
			J
	1201967		
Signatory above	ing this form, ASIC should be	contact (Choose one of the following)	
ASIC registered a	gent above		
人 Name of lodging p	party:		
ANTISS	USE THERAPE	MICS UMITED	
Office, unit, level, o			
Leve		unione de de la companya de la laboración de la companya de la companya de la companya de la companya de la co	
Street number and			
le w	ALLACE AVEN	L.	
Suburb/City		State/Temtory :	
TOOK	AV	VIC	
Postcode	Country (if not Australia)		
3142	DV COVERY		
DX Number	DX City/subur		
Telephone Numbe			
०२ ५४	^ -		



Mail

Send completed and signed forms to: Australian Securities and Investments Commission, PO Box 4000, Gippsland Mail Centre VIC 3841. For help or more information

Telephone

03 5177 3988

Email

info.enquiries@asic.gov.au

Web

www.asic.gov.au/easylodge

24 July 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

## Antisense Therapeutics to Initiate "Proof of Concept" Study for Psoriasis Project

## **Progress to Date**

Antisense Therapeutics has recently made a series of important announcements with respect to the progress of its psoriasis project (ATL1101):

- In May this year the company announced the approval of a \$1.1 million Commonwealth Government Start Grant to assist the company to develop its psoriasis treatment.
- In June, the company announced the achievement of a significant milestone with the demonstration that a cream containing ATL1101 can penetrate human psoriasis skin biopsies in the laboratory and silence the target gene IGF-1r (which is a receptor protein found in excessive amounts in actively dividing cells of psoriatic skin). This laboratory result provided us with increased confidence that ATL1101 may be effective as a topical cream formulation to treat psoriasis.

## "Proof of Concept" Study

The company is now pleased to advise that it will undertake an important "proof of concept" study which is an accelerated path to testing the activity of ATL1101 in humans suffering from psoriasis.

In this "proof of concept" study, also referred to as the Small Plaque Assay (SPA), ATL1101 will be topically applied to a limited number of patients in relatively small quantities to defined areas of psoriatic skin. The SPA is designed to carefully monitor and also restrict the extent of patients' exposure to the test compound.

Typically a drug's activity is not established until completion of Phase II clinical trials. However, a "proof of concept" study can be undertaken relatively inexpensively for a disease such as psoriasis (unlike for many other diseases), which will provide early evidence of the effectiveness of ATL1101. While the SPA will not replace the requirement to undertake formal (Phase I, II and III) human clinical trials, if early indications of the drug's effectiveness are shown, the company will have:

- increased confidence in the prospects for successful commercial development of ATL1101;
- excellent data to pursue potential early partnering opportunities.

## **Timing of Study**

Planning of the SPA is well advanced with the identification of the manufacturer of ATL1101, and selection of the contract research organisation to conduct the SPA.

The manufacture of the drug product and the required precursory toxicology program are expected to be completed in the first half of 2004, after which an application for approval to commence the study may be submitted. Once this approval is received, the "proof of concept" study in psoriasis patients should commence in mid to late 2004.

## **Background Information**

*Psoriasis* is a chronic, non-contagious skin disorder, which affects 2% of the population. While the precise cause of psoriasis is unknown, it is thought to be triggered by an immune system defect leading to excessive skin cell division. The worldwide market for psoriasis treatments was more than US\$500 million in 2000 and there is an acknowledged unmet medical need for more effective and safer treatments. The market is forecast to grow to beyond US\$2 billion with the emergence of new therapies.

Antisense drugs are synthetic, DNA-like compounds designed for use as medicines, which block disease processes with extraordinary precision. Unlike conventional small-molecule medicines, the discovery of which requires time-consuming and laborious trial-and-error, antisense medicines are rationally designed by directly exploiting the huge body of genetic information now available from the human genome project. There are currently over 20 antisense drugs in clinical trials worldwide to treat various diseases, with more than half of these in Phase II or later stage clinical development. While there is already one antisense drug approved for clinical use, it is anticipated that several more will enter the market over the next few years.

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company (ASX: ANP). The company's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102) and Psoriasis (ATL1101). Antisense plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies. The company's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Contact Information:

Website: www.antisense.com.au

Managing Director - Mark Diamond +61 3 9827 8999

Company Secretary - Natalie Korchev +61 3 9827 8999

2004 HOV 16 P 12: 18

OFFICE OF INTERNATIONS -CORPORATE FIRMINGS

Rule 4.7B

## **Appendix 4C**

## Quarterly report for entities admitted on the basis of commitments

Introduced 31/3/2000. Amended 30/9/2001

• •	_		. • .
Name	nτ	en	titu
	•	~**	.,,,

## ANTISENSE THERAPEUTICS LIMITED

ABN

41 095 060 745

Quarter ended ("current quarter")

30 JUNE 2003

## Consolidated statement of cash flows

Cash flows related to operating activities		Current quarter	Year to date (12 months)	
		•	\$A'000	\$A'000
1.1	Receipts from c	ustomers	-	-
1.2	Payments for	(a) staff costs	(248)	(1,000)
		<ul><li>(b) advertising and marketing</li><li>(c) research and development</li></ul>	(972)	(5,798)
		(d) leased assets (e) other working capital	(182)	(736)
1.3	Dividends recei	ved	-	-
1.4	Interest and o	ther items of a similar nature	60	351
1.5		er costs of finance paid	-	-
1.6	Income taxes pa		-	-
1.7	Other (provide - Insurance ref	details if material) und	2	2
	- GST received	I from ATO	21	180
	Net operating	cash flows	(1,319)	(6,998)

<sup>+</sup> See chapter 19 for defined terms.

		Current quarter \$A'000	Year to date (twelve months) \$A'000
1.8	Net operating cash flows (carried forward)	(1,319)	(6,998)
	Cash flows related to investing activities		
1.9	Payment for acquisition of:		-
	(a) businesses (item 5) (b) equity investments	-	-
	(c) intellectual property	-	-
	(d) physical non-current assets	(9)	(23)
	(e) other non-current assets	-	-
1.10	Proceeds from disposal of:		
	(a) businesses (item 5)	-	-
	(b) equity investments	-	-
	(c) intellectual	-	-
	property	-	-
	(d) physical non- current assets	-	-
	(e) other non-current assets	-	-
1.11	Loans to other entities	-	-
1.12	Loans repaid by other entities	-	-
1.13	Other (provide details if material)	-	-
	Net investing cash flows	(9)	(23)
1.14	Total operating and investing cash flows	(1,328)	(7,022)
	Cash flows related to financing activities		
1.15	Proceeds from issues of shares, options, etc.	_	4,521
1.16	Proceeds from sale of forfeited shares	-	-
1.17	Proceeds from borrowings	•	-
1.18	Repayment of borrowings	- ]	-
1.19 1.20	Dividends paid Other - costs relating to issue of shares		(327)
	Net financing cash flows	_	4,194
	Not increase (decrease) in each hold	(1 220)	
	Net increase (decrease) in cash held	(1,328)	(2,827)
1.21	Cash at beginning of quarter/year to date	7,873	9,373
1.22	Exchange rate adjustments to item 1.20		-
1.23	Cash at end of quarter	6,546	6,546

Appendix 4C Page 2 30/9/2001

<sup>+</sup> See chapter 19 for defined terms.

## Payments to directors of the entity and associates of the directors Payments to related entities of the entity and associates of the related entities

		Current quarter \$A'000	
1.24	Aggregate amount of payments to the parties included in item 1.2	916	
1.25	Aggregate amount of loans to the parties included in item 1.11	-	
1.26	Explanation necessary for an understanding of the transactions		
	Item 1.24 Reflects the following related party payments:  (a) Total amounts paid to directors include director's fees, salarie	s and superannuation of \$77,083	

- (YTD: \$401,177).
- (b) Dr Stanley Crooke, a director of the Company is also a director of Isis Pharmaceuticals Inc ("Isis"). A total amount of \$216,365 (YTD: \$3,542,838) was paid to Isis for research and development related services provided by them to Antisense Therapeutics Limited ("ATL").
- (c) Professor George Werther, a director of the company, is an executive officer of the Murdoch Childrens Research Institute ("MCRI"). An amount of \$622,564 (YTD: \$1,399,558) was paid to the MCRI for research services performed by them for ATL.

IN	on-cash financing and investing activities	
2.1	Details of financing and investing transactions which have had a material effect on consolidated assets and liabilities but did not involve cash flows	
	Not applicable.	
2.2	Details of outlays made by other entities to establish or increase their share in businesses in which the reporting entity has an interest	
	Details of outlays made by other entities to establish or increase their share in businesses in which the reporting entity has an interest	

## Financing facilities available

Add notes as necessary for an understanding of the position. (See AASB 1026 paragraph 12.2).

		Amount available \$A'000	Amount used \$A'000
3.1	Loan facilities	-	-
3.2	Credit standby arrangements	-	-

30/9/2001 Appendix 4C Page 3

<sup>+</sup> See chapter 19 for defined terms.

## Reconciliation of cash

Reconciliation of cash at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts is as follows.		Current quarter \$A'000	Previous quarter \$A'000
4.1	Cash on hand and at bank	1,546	2,873
4.2	Deposits at call	5,000	5,000
4.3	Bank overdraft	-	-
4.4	Other (provide details)	-	-
	Total: cash at end of quarter (item 1.23)	6,546	7,873

## Acquisitions and disposals of business entities

		Acquisitions (Item 1.9(a))	Disposals (Item 1.10(a))	
5.1	Name of entity	Not applicable	Not applicable	
5.2	Place of incorporation or registration			
5.3	Consideration for acquisition or disposal			
5.4	Total net assets			
5.5	Nature of business			

## Compliance statement

- 1 This statement has been prepared under accounting policies which comply with accounting standards as defined in the Corporations Act (except to the extent that information is not required because of note 2) or other standards acceptable to ASX.
- 2 This statement does /does not\* (delete one) give a true and fair view of the matters disclosed.

Sign here:		Date: 31 July 2003
-	Company secretary	·

Print name: Natalie Korchev

Appendix 4C Page 4

30/9/2001

<sup>+</sup> See chapter 19 for defined terms.

## **Notes**

- 1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity wanting to disclose additional information is encouraged to do so, in a note or notes attached to this report.
- 2. The definitions in, and provisions of, AASB 1026: Statement of Cash Flows apply to this report except for the paragraphs of the Standard set out below.
  - 6.2 reconciliation of cash flows arising from operating activities to operating profit or loss
  - 9.2 itemised disclosure relating to acquisitions
  - 9.4 itemised disclosure relating to disposals
  - 12.1(a) policy for classification of cash items
  - 12.3 disclosure of restrictions on use of cash
  - 13.1 comparative information
- 3. Accounting Standards. ASX will accept, for example, the use of International Accounting Standards for foreign entities. If the standards used do not address a topic, the Australian standard on that topic (if any) must be complied with.

30/9/2001 Appendix 4C Page 5

<sup>+</sup> See chapter 19 for defined terms.



SECTIVED

SESSIFIED

S

13 August 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Updated Corporate Presentation

Please find attached Antisense Therapeutics Limited's updated company presentation.

Yours sincerely

Natalie Korchev Company Secretary



(ASX : ANP)



# antisense pharmaceuticals for large unmet Create, develop and commercialize novel markets.



♦ Listed on ASX Dec 2001 – oversubscribed

Successful 2<sup>nd</sup> round funding in Dec 02

Market Capitalization: A\$40M (undiluted)

Key Shareholders

24%

- Circadian

- Syngene

20% (42% Circadian)

15%

- QIC

- Isis

2%

4%

- MCRI



# Bob Moses, Chairman (ex VP of CSL)

- Mark Diamond, CEO (ex Faulding)
- Dr Chris Belyea (CEO Metabolic)
- Dr Stanley Crooke (Founder ISIS Pharmaceuticals)
- Prof Graham Mitchell (Foursight/CSL)
- Prof George Werther (MCRI)



# Leverage 13 years of Isis antisense technology development

- Fast track existing lead projects through pre-clinical and clinical development
- Create pipeline of new antisense therapeutics
- clinical testing via licensing/partnering Commercialize projects successful in



## Antisense Therapeutics

- Acknowledged global leader in antisense
- Over US \$1B invested in antisense chemistries
- More than 1,000 patents issued
- 1 FDA drug approved, 8 in late stage clinical development
- Deals with large market cap companies (eg Lilly and Amgen)
- Lilly deal (US\$200m committed cash)



# 31 December 2002 – Financial Summary

# Balance Sheet - Extract

Cash assets

Intangible asset

Payables

Net Assets

A\$ 10.0 m

A\$ 5.1 m A\$ (1.9) m A\$ 13.8 m

*30 June 2003:* 

Cash assets

A\$ 6.5 m



# 31 December 2002 – Financial Summary (cont)

## Profit & Loss

Half year operating loss of A\$3.9 m is after (charging)/crediting:

Research and development

Amortization of intangible

Interest income

Overheads, patent costs & other

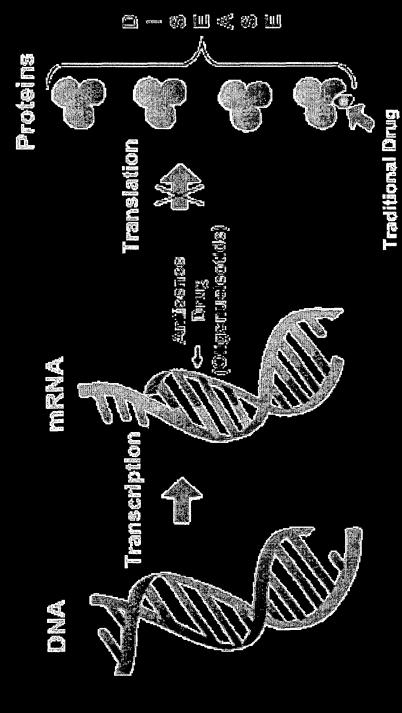
A\$ (2.8) m

A\$ (0.6) m A\$ 0.2 m A\$ (0.7) m



# A fundamentally different approach to making medicine

- Unprecedented target specificity and selectivity
- activity of proteins that cause disease Most current drugs interfere with the
- block the manufacture of the target protein Antisense drugs go to work earlier, they



Antisense Therapeutics

....Blocks disease-causing proteins from being produced



## soituegrahT eznezitnA

- Mature technology (20 years in development)
- Drug discovery and research is faster and more predictable
- Compounds are potentially more selective, effective and less toxic
- Broad disease application
- Dosing advantages (route and frequency)



# Disease & Market

- Chronic non-contagious skin disorder
- Affects 1-2% of population
- Global drug sales over US\$500 million in 2000
- Need for more effective therapies

## Product

- Antisense inhibitor to IGF-1R regulates cell growth
- Developing topical formulation



## soituegeredT eeneeitnA

## Progress

- Selected antisense lead inhibitor
- Prepared topical formulation
- Confirmed cream active in psoriasis skin
- Completed pre-clinical efficacy program
- Awarded A\$1.1 million government START grant

## Outlook

- Commence "Proof of Concept" study in psoriasis patients in 2004



# Disease & Market

- Life-long chronic disease of the central nervous system
- Global drug sales of > US\$2.5bn in 2002
- Need for more effective drug with less side effects

## Product

- Antisense inhibitor to VLA-4 protein which contributes to onset of disease
- Biogen monoclonal ab to VLA-4 in Phase III
- Anticipate efficacy, dosing and cost advantages



## Progress

- Activity in pre-clinical murine models of MS
- Activity also in arthritis and asthma models
- Completed package of pre-clinical animal studies (incl. toxicology)

Antisense Therapeutics

- Submitted 'IND' for Phase I trials
- Received approval to commence Phase I trial
- Manufactured drug product for Phase I and IIa studies



## Outlook

 Phase I human trial dosing to start September 2003 in UK.

eaifuegarahT eaneaifnA

 Following successful completion of Phase I trial, Phase IIa trials in 2004



## Concl "PoC" By end 2005 Concl Ph IIa 1st half'04 2nd half'04 2nd half'04 1st half'04 Timing Ongoing Complete product manufacture Start "Proof of Concept" study studies with new antisense leads compound at pre-clinical stage Complete multiple animal Objective: to partner a and toxicology program Partnering objective Partnering objective Complete Phase I Start Phase IIa Value Driver (Psoriasis) ATL1102 ATL1101 Research Project Pipeline (MS)

Antisense Therapeutics





## MARKET RELEASE

18 August 2003

## **Antisense Therapeutics Limited**

## TRADING HALT

The securities of Antisense Therapeutics Limited (the "Company") will be placed in pre-open at the request of the Company, pending the release of an announcement by the Company. Unless ASX decides otherwise, the securities will remain in pre-open until the earlier of the commencement of normal trading on Wednesday, 20 August 2003 or when the announcement is released to the market.

Security Codes:

ANP, ANPO

Dean Litis

Senior Companies Adviser





20 August 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000



Dear Sir/Madam

Re: Share Placement

The Directors of Antisense Therapeutics Limited (ASX: ANP) advise that the company has completed a placement of shares to Australian institutions and sophisticated investors, raising \$5 million by the issue of 38.5 million shares at \$0.13 per share. The placement, which was managed by ABN Amro Morgans Limited, was well supported by existing shareholders as well as a number of new institutional investors and closed oversubscribed.

As part of the placement, existing shareholder, Circadian Technologies Limited, has agreed to subscribe for approximately \$1 million at \$0.13 per share. This is subject to shareholder approval which will be sought at the company's Annual General Meeting.

The funds raised through the placement will be applied to Antisense Therapeutics' drug development projects: ATL1102 for multiple sclerosis, ATL1101 for psoriasis and other drug discovery activities.

The Directors of the company will shortly provide an opportunity through a Share Purchase Plan (SPP) for all eligible shareholders of Antisense Therapeutics to buy additional shares in the company at the same price paid by sophisticated investors in this placement.

Yours sincerely

Natalie Korchev Company Secretary

## About Antisense Therapeutics Limited

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Further company details are available on the Antisense Therapeutics website.

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999



RECEIVED

MINOV 16 P 12: 18

EFFICE OF INTERNATIONAL
CORPORATE FINANCE

22 August 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Total number of pages: 36

Dear Sir/Madam

## Re: PRELIMINARY FINAL REPORT (APPENDIX 4E) (AUDITED) AND OPERATIONS REPORT – 30 JUNE 2003

In accordance with Listing Rule 4.1 we enclose the Preliminary Final Report (Appendix 4E) (audited) on the results of Antisense Therapeutics Limited ('Antisense Therapeutics') for the year ended 30 June 2003.

The Directors report a loss after income tax for the period of \$6,107,898 (2002: \$6,321,006). The loss is after fully expensing all research and development costs. Antisense Therapeutics has no borrowings and has cash and bank term deposits as at 22 August 2003 amount to \$10.8 million.

The company has made substantial progress in its Research and Development activities over the period under review with a focus on meeting the key project milestones for its lead compounds, ATL1102 and ATL1101. The major achievements announced by the company were:

## Multiple Sclerosis Project (ATL1102)

- The successful completion of a package of pre-clinical animal trials of ATL's drug for the treatment of multiple sclerosis, ATL1102;
- Confirmation of the site for Phase I clinical trials for ATL1102 and receipt of approval to conduct this trial;
- Completion of manufacture of ATL1102 for use in Phase I and later clinical trials.

## Psoriasis Treatment Project (ATL1101)

- Selection of ATL1101 lead compound for psoriasis;
- Demonstration that a cream containing ATL1101 can penetrate human psoriasis skin biopsies in the laboratory and silence the target gene IGF-1R;
- Approval of a \$1.1M grant under the Commonwealth Government's R&D Start Program to assist in the development of the psoriasis treatment.

The Company also successfully raised \$4.5 million in an oversubscribed share offer in December 2002.

Subsequent to year end, the company announced the raising of a further \$5 million by the issue of 38.5 million shares at \$0.13 per share in a placement of shares to Australian institutions and professional investors.

Further details regarding the progress of the company's operations are provided in the Operations Report included in the Appendix 4E attached.

This letter and the attached Appendix 4E Preliminary Final Report form part of this announcement to the Australian Stock Exchange Limited.

Yours faithfully
Antisense Therapeutics Limited

Mark Diamond Managing Director

## **APPENDIX 4E**

## **Preliminary Final Report**

Name of entity:

ANTISENSE THERAPEUTICS LIMITED

ABN:

41 095 060 745

Reporting period:

FINANCIAL YEAR ENDED 30 JUNE 2003

Previous

Corresponding period:

FINANCIAL YEAR ENDED 30 JUNE 2002

## **INDEX**

- 1. Results for announcement to the market
- 2. Commentary on Results
- 3. Review of Operations Report
- 4. Financial Report
- 5. Other Information

**Note:** The financial figures provided are in <u>actual</u> Australian dollars, unless specified otherwise.

## RESULTS FOR ANNOUNCEMENT TO THE MARKET

The results of Antisense Therapeutics Limited for the year ended 30 June 2003 are as follows:

Revenues and Results from Ordinary Activities:		Change compared to 2002	2003 \$
Revenues from ordinary activities	Up by \$39,379	10%	448,066
Profit (loss) from ordinary activities after tax attributable to members	Loss has decreased by \$213,108	3%	(6,107,898)
Net profit (loss) for the period attributable to members	Loss has decreased by \$213,108	3%	(6,107,898)

#### Dividends:

No dividends have been paid or declared by the entity since the beginning of the current reporting period.

No dividends were paid for the previous corresponding period.

## Brief Explanation of figures reported above:

Revenue from ordinary activities increased in the current period due to increased interest income.

The loss from ordinary activities is after fully expensing research and development expenditure. The reduction in the loss represents the majority of the costs of the manufacture and development of the Multiple Sclerosis ATL1102 drug compound being incurred in the prior period. This decrease has been offset by a full year's amortisation of the intangible asset and a full year of administrative expenses this financial year compared with 7 months in the prior financial year.

For further details relating to the current period's results, refer to the "Commentary on Results" on the following page.

#### **COMMENTARY ON RESULTS**

(As communicated in the cover letter to this Appendix 4E)

The Directors report a loss after income tax for the period of \$6,107,898 (2002: \$6,321,006). The loss is after fully expensing all research and development costs. Antisense Therapeutics has no borrowings and has cash and bank term deposits as at 22 August 2003 amounted to \$10.8 million.

The company has made substantial progress in its Research and Development activities over the period under review with a focus on meeting the key project milestones for its lead compounds, ATL1102 and ATL1101. The major achievements announced by the company were:

#### Multiple Sclerosis Project (ATL1102)

- The successful completion of a package of pre-clinical animal trials of ATL's drug for the treatment of multiple sclerosis, ATL1102;
- Confirmation of the site for Phase I clinical trials for ATL1102 and receipt of approval to conduct this trial;
- Completion of manufacture of ATL1102 for use in Phase I and later clinical trials.

## Psoriasis Treatment Project (ATL1101)

- Selection of ATL1101 lead compound for psoriasis;
- Demonstration that a cream containing ATL1101 can penetrate human psoriasis skin biopsies in the laboratory and silence the target gene IGF-1R;
- Approval of a \$1.1M grant under the Commonwealth Government's R&D Start Program to assist in the development of the psoriasis treatment.

The Company also successfully raised \$4.5 million in an oversubscribed share offer in December 2002.

Subsequent to year end, the company announced the raising of a further \$5 million by the issue of 38.5 million shares at \$0.13 per share in a placement of shares to Australian institutions and professional investors.

Further details regarding the progress of the company's operations are provided in the Operations Report which follows.

#### **OPERATIONS REPORT**

#### Overview of Company's Activities

The company has made substantial progress in its Research and Development activities over the period under review with a focus on meeting the key project milestones for its lead compounds, ATL1102 and ATL1101. The major achievements announced by the company were:

#### Multiple Sclerosis Project (ATL1102)

- The successful completion of a package of pre-clinical animal trials of ATL's drug for the treatment of Multiple Sclerosis, ATL1102;
- Confirmation of the site for Phase I clinical trials for ATL1102 and receipt of approval to conduct this trial;
- Completion of manufacture of ATL1102 for use in Phase I and later clinical trials.

### Psoriasis Treatment Project (ATL1101)

- Selection of ATL1101 lead compound for Psoriasis;
- Demonstration that a cream containing ATL1101 can penetrate human Psoriasis skin biopsies in the laboratory and silence the target gene IGF-1R;
- Approval of a \$1.1M grant under the Commonwealth Government's R&D Start Program to assist in development of the Psoriasis treatment.

During the period the company successfully raised \$4.5 million in an oversubscribed share offer. On 20 August 2003, the company announced the raising of a further \$5 million in a share placement to Australian institutions and professional investors.

#### Antisense Therapeutics' Mission

ATL's mission is to create, develop and commercialise novel antisense pharmaceuticals. Our primary focus is to progress our two lead compounds (ATL1102 and ATL1101) through research and clinical trials with the aim of providing new and improved therapies for the treatment of Multiple Sclerosis and Psoriasis respectively, and to support these lead compounds by building a pipeline of additional antisense compounds.

#### Antisense Technology - How It Works

Proteins play a central role in virtually every aspect of human biology. Each of our genes is a set of instructions for, and control of, the manufacture inside the cell of a particular unique protein. Conventional pharmaceutical drugs typically bring about their desired therapeutic effect by binding to a target protein directly, to interfere with its action.

Antisense drugs are synthetic, DNA-like compounds designed for use as medicines, which block disease processes with extraordinary precision. Unlike conventional small-molecule medicines, the discovery of which requires time-consuming and laborious trial-and-error, antisense medicines are rationally designed by directly exploiting the huge body of genetic information now available from the human genome project. Compared to conventional drugs antisense aims to provide faster, more predictable drug discovery, with increased specificity of action and uniformity of methods of manufacture, formulation and delivery.

Antisense drugs have the potential to treat a wide range of conditions and diseases including autoimmune, infectious, inflammatory, dermatological, metabolic and cardiovascular diseases as well as cancer. There are currently over 20 antisense drugs in clinical trials worldwide to treat various diseases, with more than half of these in Phase II or later stage clinical development. While there is already one antisense drug approved for clinical use, it is anticipated that several more will enter the market over the next few years.

#### **Overall Operating Strategy**

ATL's strategy is:

- to gain access to the best enabling antisense technologies through partnership with key antisense technology leaders;
- to create candidate antisense drugs for diseases where there are large and/or poorly met markets, in collaboration with ATL's technology and research partners;
- to out-source pre-clinical and clinical testing of the candidate drugs to expert contractors; and
- to commercialise the drugs that are shown to be successful through licensing deals or other partnerships with major pharmaceutical companies.

The company's "virtual structure" minimises infrastructure and overhead costs. This is achieved by working with contractors and consultants on a worldwide basis in order to gain access to the best possible expertise in each area of the company's development operations. These outsourcing activities are closely controlled by the company's management who have extensive experience in the research and clinical development of pharmaceutical products.

A key aspect to the company's out-sourcing strategy is the collaborations it has developed with Isis Pharmaceuticals Inc ("Isis") and the Murdoch Childrens Research Institute ("MCRI") who are at the same time major shareholders in ATL. The company has made substantial technical progress with its developments over the period under review due to the commitment and expertise of its collaboration partners.

### Isis Strategic Partnership

A fundamental element of the ATL strategy is its access to state of the art antisense technology, both in respect of know-how and intellectual property to accelerate drug discovery and development. As a leader in the field, Isis is the ideal technology partner for ATL. Isis currently has one antisense drug on the market (VitraveneTM) and seven compounds in late stage clinical development. Isis has several partnerships with major pharmaceutical companies.

The collaboration agreement with Isis provides ATL with an extensive package of access to Isis's antisense drug discovery technology to commercialise antisense drugs to a number of protein targets including IGF-1R for Psoriasis and an exclusive license to ATL1102, which ATL is currently progressing into clinical development for Multiple Sclerosis. Isis has already manufactured batches of bulk drug product and will be available to manufacture further quantities for use in clinical trials for ATL.

The collaboration agreement with Isis also provides access to and assistance in expanding ATL's drug pipeline including the rapid generation of antisense lead compounds to the Company's potential therapeutic targets.

#### MCRI Strategic Collaboration

The MCRI, based at the Royal Children's Hospital in Melbourne is a major Australian research institute with over 450 staff and operates as an independent non-profit organisation.

ATL has entered into agreements with the MCRI by which it has obtained the exclusive worldwide rights to commercialise antisense drugs for Psoriasis and other skin diseases. As part of its research agreement with ATL, the MCRI provides scientific support of the pre-clinical and clinical development, including laboratory testing of the Isis-generated drugs and formulations. MCRI is also generating laboratory data on antisense treatments in other skin disorders.

## **Projects Update**

Multiple Sclerosis: ATL1102

#### Background

Multiple Sclerosis (MS) is a life-long, chronic, incurable disease, which progressively destroys the central nervous system, commonly diagnosed between the ages of 20 and 40 years. The disease affects about 400,000 people in the US where the estimated annual healthcare cost associated with the disease in 2002 was US\$2.5 billion. Although current treatments are unable to slow disease progression, the aims of therapy are to reduce the duration, frequency and severity of the attacks.

The development of improved Multiple Sclerosis medications is a high opportunity area. There is no cure for MS – the goals of therapy are to improve recovery from attacks, to prevent or lessen the number of relapses and their severity, and to reduce disease progression. Until recently steroids were the principal medications for MS – while steroids cannot affect the progression of MS, they can reduce the duration of attacks. Interferon beta drugs appeared on the market in the early 1990's, but their longer-term therapeutic benefits are unclear.

ATL1102 is a drug under development by ATL, which aims to prevent the synthesis of a protein called VLA-4, known to play a part in both the onset and progression of MS.

Clinical evidence for VLA-4 target activity in Multiple Sclerosis has been demonstrated by the monoclonal antibody drug, Antegren<sup>TM</sup>, currently being developed by US based biopharmaceutical company, Biogen, which is being assessed in Phase III human trials. By contrast to acting on the VLA-4 protein after it is produced, ATL1102 is designed to block the production of that disease causing protein before it can inflict further damage. Advantages of ATL1102 over an antibody product may potentially include efficacy, dosing route and cost of therapy.

#### **Progress**

In October 2002, ATL announced the successful completion of a package of preclinical (animal) studies, which enabled ATL to submit an application to the Charterhouse Clinical Research Unit at the Stamford Hospital in London ("Charterhouse") to conduct a Phase I clinical trial to assess the safety and disposition (pharmacokinetics) of ATL1102 in human volunteers. Approval was received from Charterhouse in February 2003 to conduct this Phase I study.

The production of injectable formulations of ATL1102 suitable for use in Phase I clinical trials was contracted out to a FDA compliant US manufacturer. Although unforeseen events in the manufacturing process led to delays, the manufacture is now complete.

As required by regulations, the manufactured formulations underwent full quality testing at a contract organisation in the USA. Quality testing involves the evaluation of the formulated product to ensure it meets product specifications. This program of work was completed in August 2003 and the products have been certified for 'release'. The formulations have been shipped to Charterhouse in London to commence the Phase I clinical trial, which is scheduled to commence in late August 2003.

#### Outlook

Upon successful completion of the Phase I clinical trial, it is anticipated that an application will be made in 2004 for a Phase IIa trial to assess preliminary efficacy in patients with MS.

#### Psoriasis: ATL1101

#### Background

Psoriasis is a chronic non-contagious skin disorder, which affects around 2% of the population. While the precise cause of Psoriasis is unknown, it is thought to be triggered by an immune system defect leading to excessive skin cell division. When severe, 15-20% of the person's body may be affected. The white scales that usually cover the lesion are composed of dead skin cells, and the redness of the lesion is caused by increased blood supply to the area of rapidly dividing skin cells.

The worldwide market for Psoriasis treatments was valued at US\$500 million in 2002 and there is an acknowledged unmet medical need for more effective and safer treatments. The market is forecast to grow beyond US\$2 billion by 2007 ("Frost & Sullivan") with the emergence of new effective treatments.

In the absence of a cure, the goal for a Psoriasis treatment is to reduce inflammation and/or to slow down rapid skin cell division to decrease the extent of skin lesions. While there are a number of treatments on the market today, most have limited efficacy or side-effect profiles, which restrict their usefulness. There is a range of new treatments undergoing clinical trials, some of which should be expected to reach the market. These include systemic injected drugs based on monoclonal antibodies designed to interfere with specific parts of the immune system thought to be important in the development of Psoriasis. Whether any of these drugs will offer an improvement to existing therapies is not yet known. Despite the wide range of current treatment choices and the treatments in development, 2% of the world's population awaits an effective treatment for Psoriasis.

ATL1101 is an antisense drug designed to silence the gene for the insulin-like growth factor-I receptor (IGF-Ir). IGF-Ir's pivotal role in the regulation of cell overgrowth in Psoriasis was established by our research partner, the Murdoch Childrens Research Institute. ATL1101 is being developed for topical application and is intended as a first line therapy.

#### **Progress**

The ATL1101 lead compound was selected in the third quarter of 2002 on schedule and a topical formulation containing ATL1101 was prepared using Isis Pharmaceuticals, Inc proprietary formulation expertise.

A significant milestone was achieved in the second quarter of 2003 with the demonstration that the cream containing ATL1101 can penetrate human Psoriasis skin biopsies in the laboratory and silence the target IGF-Ir. The laboratory result provided increased confidence that ATL1101 may be effective as a topical cream formulation to treat Psoriasis.

In May 2003, the Psoriasis project was awarded a grant under the Commonwealth Government R&D Start Program. The grant will provide \$1.1M in dollar-for-dollar funding for the financial year 2003/2004. The awarding of this grant provides validation of the scientific, clinical and commercial potential of the Psoriasis project.

The research team at the MCRI has also been actively investigating the application of ATL1101 in other skin disorders. Laboratory experiments to confirm the potential effectiveness of ATL1101 in these disorders are well advanced. The company will announce details of these investigations once the data has been generated and assessed.

#### Outlook

The next stage of development for ATL1101 is the undertaking of a "proof of concept" study which is an accelerated path to testing the activity of ATL1101 in humans suffering from Psoriasis.

In this "proof of concept" study, also referred to as the Small Plaque Assay (SPA), ATL1101 will be topically applied to a limited number of patients in relatively small quantities to defined areas of psoriatic skin. The SPA is designed to carefully monitor and also restrict the extent of patients' exposure to the test compound.

Typically a drug's activity is not established until completion of Phase II clinical trials. However, a "proof of concept" study can be undertaken relatively inexpensively for a disease such as Psoriasis (unlike for many other diseases), which will provide early evidence of the effectiveness of ATL1101. While the SPA will not replace the requirement to undertake formal (Phase I, II and III) human clinical trials, if early indications of the drug's effectiveness are shown, the company will have increased confidence in the prospects for successful commercial development of ATL1101, and excellent data with which to pursue potential early partnering opportunities.

The manufacture of the drug product and the required precursory toxicology program are expected to be completed in the first half of 2004, after which an application for approval to commence the SPA may be submitted. Once this approval is received, the "proof of concept" study in Psoriasis patients should commence in mid to late 2004.

#### Other Research Projects

#### Background

The company has agreed a list of exciting research targets with Isis, and can during the research and development phase, select a certain number of those with the most potential to exclusively commercialise. ATL is focusing on potential therapeutic drug targets from published scientific and clinical research where ATL's analysis shows that these targets may be suitable for intervention with antisense drugs and where an antisense drug may have an advantage over existing treatments or those in development.

As stated earlier, ATL has acquired from Isis an exclusive right to research these targets using the Isis technology, and in accordance with the ATL/Isis contracts, antisense compounds to these targets are being created by Isis for ATL. ATL are contracting with local and international expert groups to assess the efficacy of these antisense compounds in the relevant animal models. When efficacy in animals is established, ATL will elevate the most promising drugs to its development pipeline for trials in humans.

#### Progress

ATL has research projects on its pipeline antisense inhibitors at various stages of completion in animal disease models. Early indications are that at least one of these compounds has shown efficacy comparable to leading therapies for its given disease indication; studies in other disease areas are underway. All disease indications under investigation at ATL have significant unmet therapeutic markets, and with the inherent safety and dosing advantages of antisense drugs over conventional therapies, we believe our pipeline research activities may generate interest once follow-up studies and patent filings have been completed.

It is important to note that these research outcomes can be achieved in a highly expeditious manner and at a relatively low cost, which is a key feature of utilizing the 2<sup>nd</sup> generation antisense chemistry available to us via our strategic collaboration with Isis.

#### Outlook

Following completion of the efficacy studies currently in progress and additional pilot efficacy studies during the 2003/2004 financial year, a select number of successful candidates may then be progressed into formal pre-clinical development. ATL intends to announce details of the specific disease indications together with the lead compounds once relevant patent applications have been lodged.

ATL will critically assess the results of these studies and determine on a case by case basis whether further development work will be undertaken by ATL or alternatively out-license to other pharmaceutical companies in return for licensing income.

## **Partnering Opportunities**

As stated earlier, the company's strategy is to commercialise its drug pipeline products through collaborations with major pharmaceutical companies. Given the quality of the targets and the known commercial appeal of antisense there is likely to be potential interest in both ATL1101 and ATL1102 as they progress successfully through development. The company will discuss its technology on an ongoing basis with selected interested companies in order to broaden the awareness of its activities in preparation for potential future licensing or other partnership discussions. The company also plans to pursue partnering opportunities for select pipeline compounds that are at an earlier stage of development (pre-clinical).

#### **Financial Position**

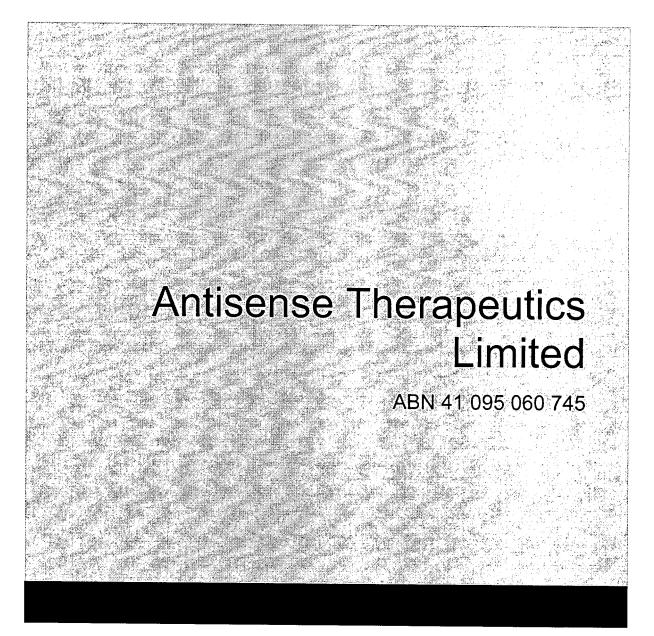
As stated in the Director's Report, the company's current cash reserves are expected to be sufficient for the planned activities until the end of 2004 if it continues to take advantage of the potential of antisense technology to move quickly from drug discovery to developing therapies (note that the company does, however, have the flexibility to delay research and development expenditure until sufficient funds are available). In order for the company to progress its projects beyond this time as described in the respective projects' "Outlook" sections, the company will be required to raise further capital.

In relation to the proposed use of funds described above, it should be recognised that there will typically be differences between the forecast and actual results, because events and circumstances frequently do not occur as expected, and those differences may be material

### Biotechnology Companies - Inherent Risks

Some of the risks inherent in the development of a product to a marketable stage include the uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of the necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Also a particular compound may fail the clinical development process through lack of efficacy or safety. Companies such as Antisense Therapeutics Limited are dependent on the success of their research projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in these areas must be regarded as speculative taking into account these considerations.

This annual report may contain forward-looking statements regarding the potential of the company's projects and interests and the development and therapeutic potential of the company's research and development. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and the financing of such activities. There is no guarantee that the company's research and development projects will be successful or receive regulatory approvals or prove to be commercially successful in the future. Actual results of further research could differ from those projected or detailed in this report. As a result, you are cautioned not to rely on forward-looking statements. Consideration should be given to these and other risks concerning the company's research and development program referred to in this Operations Report and in the company's Directors' Report as contained in this annual report for the period ended 30 June 2003.



Annual Financial Report for the year ended 30 June 2003



120 Collins Street
Melbourne, VIC 3000
Australia

GPO Box 67 Melbourne VIC 3001 Fax 61 3 9288 8000 Fax 61 3 9654 6166 DX 293 Melbourne

## Independent Audit Report

To members of Antisense Therapeutics Limited

### Scope

## The financial report and directors responsibility

The financial report comprises the statement of financial position, statement of financial performance, statement of cash flows, accompanying notes to the financial statements, and the directors' declaration for Antisense Therapeutics Limited, for the year ended 30 June 2003.

The directors of the company are responsible for preparing a financial report that gives a true and fair view of the financial position and performance of the company, and that complies with Accounting Standards, in accordance with the Corporations Act 2001. This includes responsibility for the maintenance of adequate accounting records and internal controls that are designed to prevent and detect fraud and error, and for the accounting policies and accounting estimates inherent in the financial report.

## Audit approach

We conducted an independent audit of the financial report in order to express an opinion on it to the members of the company. Our audit was conducted in accordance with Australian Auditing Standards in order to provide reasonable assurance as to whether the financial report is free of material misstatement. The nature of an audit is influenced by factors such as the use of professional judgement, selective testing, the inherent limitations of internal control, and the availability of persuasive rather than conclusive evidence. Therefore, an audit cannot guarantee that all material misstatements have been detected.

We performed procedures to assess whether in all material respects the financial report presents fairly, in accordance with the Corporations Act 2001, Accounting Standards and other mandatory financial reporting requirements in Australia, a view which is consistent with our understanding of the company's financial position, and of its performance as represented by the results of its operations and cash flows.

We formed our audit opinion on the basis of these procedures, which included:

- examining, on a test basis, information to provide evidence supporting the amounts and disclosures in the financial report, and
- assessing the appropriateness of the accounting policies and disclosures used and the reasonableness of significant accounting estimates made by the directors.

While we considered the effectiveness of management's internal controls over financial reporting when determining the nature and extent of our procedures, our audit was not designed to provide assurance on internal controls.

We performed procedures to assess whether the substance of business transactions was accurately reflected in the financial report. These and our other procedures did not include consideration or judgement of the appropriateness or reasonableness of the business plans or strategies adopted by the directors and management of the company.



## Independence

We are independent of the company, and have met the independence requirements of Australian professional ethical pronouncements and the Corporations Act 2001. In addition to our statutory audit work, we were engaged to undertake the services disclosed in the notes to the financial statements. The provision of these services has not impaired our independence.

## Audit opinion

In our opinion, the financial report of Antisense Therapeutics Limited is in accordance with:

- (a) the Corporations Act 2001, including:
  - (i) giving a true and fair view of the financial position of Antisense Therapeutics
    Limited at 30 June 2003 and of its performance for the year ended on that date; and
  - (ii) complying with Accounting Standards in Australia and the Corporations Regulations 2001; and
- (b) other mandatory professional reporting requirements in Australia.

## Inherent Uncertainty Regarding Continuation of Going Concern

Without qualification to the opinion expressed above, your attention is drawn to the following matter set out in Note 1(b) to the financial statements. As a result of the matters described in Note 1(b), because of the development stage of the company's operations and the need for future capital raisings, there is significant uncertainty whether the company will be able to continue as a going concern and therefore whether it will realise its assets and extinguish its liabilities in the normal course of business and at the amounts stated in the financial report. The financial report does not include adjustments relating to the recoverability and classification of recorded asset amounts or to the amounts and classifications of liabilities that might be necessary should the company not continue as a going concern.

Ernst & Young

Denis Thorn Partner

Melbourne

22 August 2003

# **Statement of Financial Position**

AT 30 JUNE 2003	Note	2003 \$	2002 \$
CURRENT ASSETS			
Cash assets Receivables Other	14(a) 3 4	6,545,567 68,730 878,941	9,373,050 53,196 140,030
Total Current Assets		7,493,238	9,566,276
Non-Current Assets Plant & equipment Intangible assets Total Non-Current Assets	5 6	50,911 4,438,000 4,488,911	52,440 5,715,500 5,767,940
Total Assets		11,982,149	15,334,216
CURRENT LIABILITIES  Payables Provisions Tax liabilities	7 8	326,302 38,101	1,837,089 15,415
Total Current Liabilities		364,403	1,852,504
Total Liabilities		364,403	1,852,504
Net Assets		11,617,746	13,481,712
EQUITY			
Contributed equity Reserves Accumulated losses	9 10 11	23,714,504 725,885 (12,822,643)	19,470,572 725,885 (6,714,745)
Total Equity		11,617,746	13,481,712

## **Statement of Financial Performance**

FOR THE YEAR ENDED 30 JUNE 2003	Note	2003 \$	2002 \$
Revenue from ordinary activities	2	448,066	408,687
Administrative expenses		(1,470,924)	(781,132)
Occupancy expenses		(46,829)	(24,638)
Patent expenses		(25,295)	(36,220)
Research and development expenses		(3,728,617)	(5,132,420)
Research and development expenses - amortisation			
of intellectual property	2	(1,277,500)	(672,000)
Business development expenses		-	(74,568)
Borrowing costs	2	(1,519)	(4,715)
Other expenses from ordinary activities	2	(5,280)	(4,000)
Loss from ordinary activities before income tax expense		(6,107,898)	(6,321,006)
Income tax expense relating to ordinary activities	12	-	-
Loss from ordinary activities after related income tax expense		(6,107,898)	(6,321,006)
Net loss		(6,107,898)	(6,321,006)
Increase in option reserve	10	-	725,885
Share issue costs	9	(277,359)	(717,549)
Total revenues, expenses and valuation adjustments attributable to members of Antisense Therapeutics			
Limited and recognised directly in equity	!	(277,359)	8,336
Total changes in equity other than those resulting from transactions with owners as owners	,	(6,385,257)	(6,312,670)
Basic earnings per share (cents per share)	13	(2.46)	(3.81)
Diluted earnings per share (cents per share)	13	(2.46)	(3.81)

# **Statement of Cash Flows**

FOR THE YEAR ENDED 30 JUNE 2003	Note	2003 \$	2002 \$
		<b>J</b>	J
CASH FLOWS FROM OPERATING ACTIVITIES:	100.00		
Payments to suppliers, employees and for research and development		(7,351,299)	(4,394,877)
Interest received Bank finance charges Other income received		352,771 (1,488)	249,747 (4,715)
Net cash flows used in operating activities	14(b)	(7,000,016)	91,632 (4,058,213)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property, plant and equipment Proceeds from sale of plant and equipment		(23,332) 1,680	(51,539) 4,000
Net cash flows used in investing activities		(21,652)	(47,539)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from borrowings – associated entities Repayment of borrowings – associated entities		-	100,000 (138,382)
Proceeds from issue of shares and options Payment of share and option issue costs		4,521,291 (327,106)	13,589,760 (707,917)
Net cash flows from financing activities		4,194,185	12,843,461
Net increase/(decrease) in cash held		(2,827,483)	8,737,709
Cash at the beginning of the financial year		9,373,050	635,341
Cash at the end of the financial year	14(a)	6,545,567	9,373,050

## **Notes to the Financial Statements**

#### FOR THE YEAR ENDED 30 JUNE 2003

#### NOTE 1(A) STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES

#### (i) Basis of Accounting

The financial report is a general-purpose financial report, which has been prepared in accordance with the requirements of the Corporations Act 2001 including applicable accounting standards. Other mandatory professional reporting requirements (Urgent Issues Group Consensus Views) have also been complied with.

The financial report has also been prepared in accordance with the historical cost convention.

The prior year comparatives relate to the financial performance from December 2001 following listing of the company on the Australian Stock Exchange.

#### (ii) Changes in accounting policies

The accounting policies adopted are consistent with those of the previous year except for the accounting policy with respect to the employee benefits.

The entity has adopted the revised Accounting Standard AASB 1028 "Employee Benefits", which has resulted in a change in the accounting policy for the measurement of employee benefit liabilities. Previously, the consolidated entity measured the provision for employee benefits based on remuneration rates at the date of recognition of the liability. In accordance with the requirements of the revised Standard, the provision for employee benefits is now measured based on the remuneration rates expected to be paid when the liability is settled.

There has been no material impact on retained profit and employee benefit liabilities at the beginning of the year.

#### (iii) Income Tax

The financial statements apply the principles of tax-effect accounting. The income tax benefit in the Statement of Financial Performance represents the tax on pre-tax accounting loss adjusted for income and expenses never to be assessed or allowed for taxation purposes. The provision for deferred income tax liability and future income tax benefit (as disclosed, but not recognised in the Statement of Financial Position) include the tax effect of differences between income and expenses recognised in different accounting periods for book and tax purposes, calculated at the tax rates expected to apply when the differences reverse.

The future income tax benefits relating to tax losses and timing differences have not been recognised as an asset as there is no virtual certainty of realisation.

#### (iv) Goods and Services Tax

Revenues, expenses and assets are recognised net of the amount of GST except:

- where the GST incurred on a purchase of goods and services is not recoverable from the taxation authority, in
  which case the GST is recognised as part of the cost of acquisition of the asset or as part of the expense item as
  applicable; and
- receivables and payables are stated with the amount of GST included.

Cash flows arising from operating activities are included in the Statement of Cash Flows on a gross basis (i.e. including GST) and the GST component of cash flows arising from investing and financing activities, which is recoverable from, or payable to, the taxation authority are classified as operating cash flows. Commitments and contingencies are disclosed net of the amount of GST recoverable from, or payable to, the taxation authority.

#### NOTE 1(A) STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

#### (v) Plant and Equipment

Plant and equipment are measured at cost and are depreciated over their useful economic lives as follows:

	Life	Method
Equipment and furniture	3-5 years	Straight line

#### (vi) Recoverable amounts of non-current assets

All non-current assets are reviewed annually to determine whether their carrying amounts require write down to recoverable amount.

#### (vii) Research and Development

Research and development costs are expensed as incurred, except where future benefits are expected, beyond any reasonable doubt. Where research and development costs are deferred such costs are amortised over future periods on a basis related to expected future benefits. Unamortised costs are reviewed at each balance date to determine the amount (if any) that is no longer recoverable and any amount identified is written off.

Patent costs are expensed as incurred.

#### (viii) Employee Benefits

Provision is made for employee benefits accumulated as a result of employees rendering services up to the reporting date. These benefits include wages and salaries, annual leave and long service leave.

Liabilities arising in respect of wages and salaries, annual leave, sick leave and any other employee benefits expected to be settled within twelve months of the reporting date are measured at their nominal amounts based on remuneration rates which are expected to be paid when the liability is settled. All other employee benefit liabilities are measured at the present value of the estimated future cash outflow to be made in respect of services provided by employees up to the reporting date. In determining the present value of future cash outflows, the market yield as at the reporting date on national government bonds, which have terms to maturity approximating the terms of the related liability, are used.

Employee benefit expenses and revenues arising in respect of the following categories:

- wages and salaries, non-monetary benefits, annual leave, long service leave, sick leave and other leave benefits; and
- other types of employee benefits

are recognised against profits/losses on a net basis in their respective categories.

The value of the equity-based compensation scheme described in note 20 is not being recognised as an employee benefits expense.

#### (ix) Employee Option Ownership Schemes

Certain employees are entitled to participate in option ownership schemes. The details of the schemes are described in Note 20. No remuneration expense is recognised in respect of employee options issued.

### (x) Financial Instruments Included in Equity

Ordinary share capital is recorded at the amount received on issue, less any share issue costs. Ordinary share capital bears no special terms or conditions affecting income or capital entitlements of the shareholders.

## NOTE 1(A) STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

#### (xi) Financial Instruments Included in Assets

Cash in bank and short-term deposits are stated at nominal value. Interest revenue is recognised on an effective yield basis.

#### (xii) Foreign Currencies

Transactions in foreign currencies are converted to local currency at the rate of exchange ruling at the date of the transaction.

Amounts payable to and by the company outstanding at reporting date and denominated in foreign currencies have been converted to local currency using rates prevailing at the end of the financial year.

#### (xiii) Earnings per share

Basic EPS is calculated as net loss attributable to members, adjusted to exclude costs of servicing equity (other than dividends), divided by the weighted average number of ordinary shares, adjusted for any bonus element.

Diluted EPS is calculated as net loss attributable to members, adjusted for:

- costs of servicing equity (other than dividends);
- the after tax effect of dividends and interest associated with dilutive potential ordinary shares that have been recognised as expenses; and
- other non-discretionary changes in revenues or expenses during the period that would result from the dilution of potential ordinary shares;

divided by the weighted average number of ordinary shares and dilutive potential ordinary shares, adjusted for any bonus element.

#### (xiv) Operating Leases

The minimum lease payments of operating leases, where the lessor effectively retains substantially all of the risks and benefits of ownership of the leased item, are recognised as an expense on a straight-line basis.

#### (xv) Intangible assets

Intangible assets are amortised on a straight line basis over the term of the rights granted, which is currently expected to be five years. The unamortised balance of intangible assets is reviewed at each balance date and charged to the Statement of Financial Performance to the extent that applicable future benefits are no longer probable.

#### (xvi) Payables

Liabilities for trade creditors and other amounts are carried at cost, which is the fair value of the consideration to be paid in the future for goods and services received, whether or not billed to the company.

#### (xvii) Borrowing costs

Borrowing costs are expensed as incurred.

## (xviii) Contributed Equity

Issued and paid up capital is recognised at the fair value of the consideration received by the company. Any transaction costs arising on the issue of ordinary shares are recognised directly in equity as a reduction of the share proceeds received.

## NOTE 1(A) STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

## (xix) Revenue Recognition

Revenue is recognised to the extent that it is probable that the economic benefits will flow to the entity and the revenue can be reliably measured. The following specific recognition criteria must also be met before revenue is recognised:

#### Interest

Control of the right to receive the interest payment.

#### (xx) Cash and Cash Equivalents

Cash on hand and in banks and short-term deposits are stated at nominal value.

#### NOTE 1(B) INHERENT UNCERTAINTY - GOING CONCERN

This financial report has been prepared on a going concern basis. In common with start-up biotechnology companies:

- the company's operations are subject to considerable risks due primarily to the nature of research, development and commercialisation to be undertaken; and
- the going concern basis assumes that the existing cash reserves and future capital raisings will be sufficient to enable the company to successfully execute its existing and future plans.

The financial statements take no account of the consequences, if any, of the effects of unsuccessful product development or commercialisation nor of the inability of the company to obtain adequate funding. The ability of the company to realise the carrying value of the intangible asset is subject to the successful operation of the company's existing and future plans.

NOTE 2. REVENUE AND EXPENSES	2003	2002
	\$	<u> </u>
Revenues from ordinary activities:		
Interest from external parties	355,029	289,819
Foreign exchange gains:		
Unrealised	16,832	23,236
Realised	74,525	91,632
Proceeds from the disposal of plant and equipment (a)	1,680	4,000
Total revenues from ordinary activities	448,066	408,687
Expenses and Losses:		
Depreciation of:		
- Equipment and furniture	18,854	9,818
Borrowing costs:		,
- Interest and bank charges	1,519	4,715
Operating lease rentals:	,	,
Minimum lease payments	39,475	22,679
Amortisation of intangibles	1,277,500	672,000
Other expenses comprising of:		
Written down value of plant and equipment (a)	5,280	4,000
(a) Nation or disposal of last and assistant	2.000	
(a) Net loss on disposal of plant and equipment	3,600	-

	2003 \$	2002 \$
NOTE 3. RECEIVABLES (CURRENT)		
Interest receivable - bank	43,225	40,967
Input tax credits	25,351	12,075
TFN withholding tax	154	154
Total receivables	68,730	53,196
NOTE 4. OTHER ASSETS (CURRENT)		
Prepayments	873,294	136,781
Other	5,647	3,249
Total other assets	878,941	140,030
NOTE 5. PLANT AND EQUIPMENT		
Equipment and furniture at cost		
Opening balance	63,645	16,106
Additions	22,605	51,539
Disposals	(7,701)	(4,000)
Closing balance	78,549	63,645
Accumulated Depreciation		
Opening balance	(11,205)	(1,387)
Depreciation for the period	(18,854)	(9,818)
Disposals	2,421	(11.005)
Closing balance	(27,638)	(11,205)
Net book value	50,911	52,440

NOTE 6. INTANGIBLE ASSETS	2003 \$	2002 \$
Intellectual property (a) Accumulated amortisation Closing balance	6,387,500 (1,949,500) 4,438,000	6,387,500 (672,000) 5,715,500

- (a) The intangible assets relate to certain rights granted to Antisense Therapeutics Limited by Isis Pharmaceuticals Inc. and The Murdoch Childrens Research Institute upon listing of the company. The main features of the agreements with the aforementioned entities, respectively, are as follows:
  - Isis Pharmaceuticals Inc. ("Isis") has granted Antisense Therapeutics Limited rights to use Isis technology (i.e. Isis' patented technology) to commercialise antisense drugs to a number of protein targets (i.e. a research licence for each protein target). A certain number of these research licences to protein targets are also extendible to commercialisation licences.

The agreements with Isis provide access to and assistance in expanding Antisense Therapeutics Limited's drug pipeline and also provide access to and assistance in the company's development projects including an exclusive license to a multiple sclerosis drug in Isis' preclinical pipeline; access to Isis manufacturing for provision of bulk quantities of antisense compounds for clinical trials; and access to Isis' preclinical development services for a sufficient period to allow smooth technology transfer.

• Antisense Therapeutics Limited's agreement with the Murdoch Childrens Research Institute provides the company with worldwide exclusive licences to patents covering antisense directed at a certain target for dermatological applications including psoriasis. The company's agreement with the Murdoch Childrens Research Institute also provides Antisense Therapeutics Limited with scientific support in the clinical development of a compound for psoriasis and other dermatological indications, and the testing of additional antisense compounds to be directed at other dermatological protein targets.

## NOTE 7. PAYABLES (CURRENT)

Accrued expenses (unsecured) (a) (b) Superannuation payable Total current payables	326,302	1,820,499 16,590 1,837,089
(a) Accrued expenses are non-interest bearing and are normal	ly settled on 30 day terms.	
NOTE 8. PROVISIONS (CURRENT)		
Employee entitlement (annual leave)	38,101	15,415

NOTE 9. CONTRIBUTED EQUITY	2003 \$	2002
Issued and paid up capital	23,714,504	19,470,572
(a) Movement in Issued Shares		

	200	2003		2
	No of Shares	\$	No of Shares	\$
Balance at beginning of year	215,003,110	19,470,572	108,750,005	1,000,001
Issued during the year (i)	60,275,268	4,520,645	106,250,005	19,187,500
Transaction costs arising on share issues	-	(277,359)	-	(717,549)
Exercise of options	3,230	646	3,100	620
Balance at year end	275,281,608	23,714,504	215,003,110	19,470,572

- (i) The following shares were issued on 9 December 2002:
  - 39,608,602 fully paid ordinary shares at 7.5 cents per share pursuant to the Company's Offer Information Statement dated 1 November 2002.
  - 10,333,333 fully paid ordinary shares at 7.5 cents per share to Polychip Pharmaceuticals Pty Ltd, and
  - 10,333,333 fully paid ordinary shares at 7.5 cents per share to Isis Pharmaceuticals Inc.

	2003 \$	2002
NOTE 10. RESERVES	\$	\$
Option Reserve	725,885	725,885

The option reserve represents amounts received as consideration for options issued.

## (a) Movement in Option Reserve

	2003		2002	
	No of		No of	
	Options	\$	Options	\$
Balance at beginning of period	125,422,895	725,885		-
Issued during the period	•	-	125,425,995	789,760
Less costs	-	-	•	(63,875)
Exercise of options	(3,230)	-	(3,100)	-
Balance at period end	125,419,665	725,885	125,422,895	725,885

## (b) Options over Ordinary Shares

2003

			No of Option	ıs	
Date of Issue	26/02/02	19/12/01	3/12/01	15/11/01	15/11/01
On issue at beginning of year ('000)	58,972	32,500	11,950	2,000	20,000
Issued during the year ('000)	-	-	-	-	-
Exercised during the year (*000)	(3)	-	-	-	•
Expired during the year ('000)	-	-	-	-	-
Outstanding at balance date ('000)	58,969	32,500	11,950	2,000	20,000
Exercised subsequent to balance date ('000)	-	•	-	-	•
Outstanding at date of Directors' report ('000)	58,969	32,500	11,950	2,000	20,000
Number of recipients	5,081	1,240	11	1	1
Exercise price	\$0.20	\$0.20	\$0.20	\$0.20	\$0.20
Exercise period from	26 Feb 2002	19 Dec 2001	3 Dec 2001	15 Nov 2001	15 Nov 2001
To (expiration day)	1 Feb 2007	1 Feb 2007	31 Jul 2005	31 Jul 2005	30 Nov 2006
The following proportion of options vest from the dates shown:					
100%	26 Feb 2002	19 Dec 2001	-	-	15 Nov 2001
20%	•	-	1 Aug 2002	1 Aug 2002	-
40%	-	-	1 Aug 2003	1 Aug 2003	-
40%	-	-	1 Aug 2004	1 Aug 2004	-
			200	13	2002
			\$		\$
NOTE 11. ACCUMULATED LOSSES					
Accumulated losses at the beginning of the fina	ancial year		(6,714	1,745)	(393,739)
Net loss	•		(6,107		(6,321,006)
Accumulated losses at the end of the financial	year		(12,822	2,643)	(6,714,745)

	2003 \$	2002 \$
NOTE 12. INCOME TAX		
The prima facie tax, using the tax rate applicable in the country of operation, on loss differs from the income tax provided in the financial statements as follows:		
Loss from ordinary activities	(6,107,898)	(6,321,006)
Prima facie income tax benefit calculated at 30%	(1,832,369)	(1,896,302)
Tax effect of permanent and other differences:		
Research and development Amortisation of intellectual property Amortisation of equity raising costs Amount (over)/under provided in prior years Other	(77,569) 383,250 (67,360) 316,519 312	(57,138) 201,600 - (4,594) 
Income tax benefit adjusted for permanent and other differences	(1,277,217)	(1,756,246)
Benefit of tax losses not brought to account Total income tax benefit attributable to operating loss	1,277,217	1,756,246
The estimated potential future income tax benefit at period end calculated at 30% in respect of tax losses not brought to account is:	3,151,839	1,868,594

The estimated potential future income tax benefit not recognised at period end in respect of timing differences for the company amounted to \$4,082 (2002: \$1,946).

The benefits of the tax losses and timing differences will only be realised if:

- (i) the company derives future assessable income of a nature and amount sufficient to enable the benefit of the taxation deductions to be realised;
- (ii) the company continues to comply with the conditions for deductibility imposed by law; and
- (iii) there are no changes in taxation legislation adversely affecting the company in realising the benefit from the deductions for the losses.

		2003 \$	2002 \$
TON	E 13. EARNINGS PER SHARE		
Basic	c earnings per share (cents per share)	(2.46)	(3.81)
Dilut	ted earnings per share (cents per share)	(2.46)	(3.81)
(a)	Loss used in calculating basic and diluted earnings per share(numerator)	(6,107,898)	(6,321,006)
(b)	Number of Ordinary Shares Weighted average number of ordinary shares on issue used in the calculation of basic earnings per share (denominator)	248,528,386	165,885,100
(c)	Potential Ordinary Shares Not Considered Dilutive All potential ordinary shares, being options to acquire ordinary share ended 30 June 2003.	es, are not considere	d dilutive for the

(d) There have been no other conversions to, calls of, or subscription for ordinary shares or issues of potential ordinary shares since the reporting date and before the completion of this financial report

2003	2002
\$	\$

## NOTE 14. NOTES TO THE STATEMENT OF CASH FLOWS

## (a) Reconciliation of Cash

For the purpose of the Statement of Cash Flows, cash includes cash at bank and deposits at call. Cash at the end of the period as shown in the Statement of Cash Flows is reconciled to the related items in the Statement of Financial Position as follows:

Cash at bank	1,545,567	1,873,050
Term Deposits (i)	5,000,000_	7,500,000
	6,545,567	9,373,050

(i) Term deposits are with a major bank and are short term. The bank pays interest at current bank deposit rates. At year end the average rate was 4.68%

## (b) Reconciliation of the net loss after tax to the net cash flows from operations

Net loss	(6,107,898)	(6,321,006)
Non-cash items		
Unrealised foreign exchange gain	(16,832)	(23,236)
Amortisation of intangibles	1,277,500	672,000
Depreciation expense	18,854	9,818
Loss on disposal of asset	3,600	-
Changes in assets and liabilities		
Increase in current receivables	(15,534)	(140,030)
Increase in other current assets	(738,911)	(42,534)
Increase (decrease) in payables	(1,443,480)	1,771,360)
Increase in employee provisions	22,686_	15,415
Net operating cash flows	(7,000,016)	(4,058,213)

#### NOTE 15. RELATED PARTY DISCLOSURES

#### (a) Directors

The following persons held the position of director of Antisense Therapeutics Limited during the financial year:

Chris Belyea Robert Moses Graham Mitchell Stanley Crooke George Werther Mark Diamond

#### (b) Directors' share and option holdings

(b) Directors snare and option holdings	Shares/options issued	
	2003	2002
	\$	\$
(i) Ordinary share options		
Share options issued during the year		
- directly	-	9,772,500
- indirectly		20,277,000
	+	30,049,500
Share options outstanding at year end held by directors	9,772,500	9,772,500
Share options outstanding at year end held indirectly by directors	20,277,000	20,277,000
	30,049,500	30,049,500
(ii) Ordinary shares		
Ordinary shares acquired by the directors from the entity during the		
year:	26,666	425,000
- directly - indirectly	10,333,333	30,500,000
	10,359,999	30,925,000
Ordinary shares held by directors at the end of the year	451,666	425,000
Ordinary shares held indirectly by directors at the end of the year	40,833,333	30,500,000
	41,284,999	30,925,000

#### (c) Transactions and Balances with Related Parties

The following transactions and balances were held with related parties during the year ended 30 June 2003:

- (i) Dr Stanley Crooke, a director of the company is also a director of Isis Pharmaceuticals Inc ('Isis'). During the year Isis provided various research and development related services, including manufacture of compound, to the company. The company paid Isis \$3,542,839 for these services and at year end owes Isis \$117,372 for services not invoiced.
- (ii) Professor George Werther, a director of the company is an executive officer of the Murdoch Children's Research Institute ('MCRI'). During the year the MCRI provided research services in accordance with the Research Agreement entered into between the MCRI and the company. The company paid the MCRI \$1,399,557 for these services of which \$815,156 were incurred and expensed as a research and development costs. The remaining balance of \$584,401 has been treated as a prepayment at year end.
- (iii)Payments were made to Metabolic Pharmaceuticals Limited ('Metabolic') during the year as reimbursement for various administrative costs. Dr Chris Belyea, a non-executive director of the company is also the managing director of Metabolic. The total amount paid to Metabolic during the year was \$6,382.

	2003 \$	2002 \$
NOTE 16. REMUNERATION OF DIRECTORS		
Income paid or payable, or otherwise made available in respect of the		
financial year to all directors, directly or indirectly by the company:	364,625	258,112
The number of executive and non-executive directors whose income (includin within the following bands is:	g superannuation contri 2003	butions) falls
	No.	No.
	(a)	
\$0 - \$9,999	-	3
\$10,000 - \$19,999	-	3
\$20,000 - \$29,999	4	1
\$30,000 - \$39,999	1	•
\$60,000 - \$69,999	•	1
\$100,000 - \$109,999	-	1
\$210,000 - \$219,999	1	-

#### (a) No options were granted to directors and offices during the year ended 30 June 2003.

ASIC's "Media release 03-202 Valuing options for directors and executives" provides guidelines for Australian listed companies on how to value options and similar equity instruments in the disclosure of director and executive remuneration for the 30 June 2003 Directors' Report. (ASIC's guidelines do not require that options be expensed in the financial statements, only that they be disclosed in the directors' report). The guidelines provided draw on the issuance of the Australian Accounting Standards Board's Exposure Draft 108 "Share-Based Payment" (ED 108) and its equivalent the International Accounting Standards Board's Exposure Draft ED2 "Share-Based Payment" (ED 2). ED108/ED 2 provide a basis for valuing options and allocating those values over time.

ED108 /ED 2 propose that an expense be recognised in relation to options over the period from grant date to vesting date. For options that vest immediately, the value is recognised as an expense at grant date. Previous ASIC guidelines required the total value of options issued to be disclosed as part of remuneration in the year they were issued. The company made such a disclosure, as required in its 2002 directors' report and notes to the financial statements. The options issued in these years were "well out of the money" at their respective grant dates and year end date.

Options issued by Antisense Therapeutics Limited in 2002 have 3 vesting dates, for various proportions of the total issued options, during the life of the options as detailed below. Accordingly, although no options were issued during the year ended 30 June 2003, the options issued to directors in previous years, which had not vested at 1 July 2002, have been allocated a total value of \$1,720 for the current financial year and are included in the remuneration of directors above. This amount has been determined by allocating the fair value of options issued equally over the vesting periods. Currently, the amortised fair value is not recognised as an expense in the financial statements and no adjustments have been made to reflect estimated or actual forfeitures (ie. options that do not vest or are not exercised)

Details relating to options issued and the valuation basis adopted are as follows:

#### NOTE 16. REMUNERATION OF DIRECTORS (CONTINUED)

As stated in the company's 2002 annual report:

9,500,000 options were granted to directors during the 2002 financial year. "Each option entitles the holder to purchase 1 ordinary share in Antisense Therapeutics Limited at an exercise price of 20 cents". There were 2,000,000 options granted on 15 November 2001 and 7,500,000 options granted on 3 December 2001. These options granted to directors are restricted securities and are escrowed for a period of 2 years from the date of official quotation of shares offered under the first prospectus issued by the company or such other period as the Australian Stock Exchange may require. Subject to the escrow arrangements, the option holder may not exercise more than the following proportions of options on the following dates:

•	Prior to 31 July 2002	0%
•	Between 1 August 2002 and 31 July 2003	20%
•	Between 1 August 2003 and 31 July 2004	60%
•	Between 1 August 2004 and 31 July 2005	100%

These options had no market value at date of grant and are "out of the money" as at the year end (market price per share \$0.12), whereas as stated above, the options have an exercise price of 20 cents. The directors have endeavoured to estimate the fair values of the options by using the Black-Scholes options pricing formula which values each option based on the expiration date and exercise price. Based on this accepted formula each option has a negligible value of 0.00459 of a cent. The directors have adopted this valuation for the purpose of these accounts "

These options continue to be "well out of the money" as at the 2003 year end (market share price \$0.11).

#### Values of Options Issued to Directors - Assumptions

The following assumptions were used to derive a value for the options issued using the Black-Scholes options pricing formula at the 2002 financial year end date.

## **Options Granted**

	15 November 2001	3 December 2001
Dividend yield	• •	-
Expected volatility	12.34%	12.34%
Historical volatility	12.34%	12.34%
Risk-free interest rate	5.622%	5.622%
Expected life of option	*	*

<sup>\*</sup> Assumed to be total years from grant date to expiration date.

	2003 \$	2002 \$
NOTE 17. REMUNERATION OF EXECUTIVES		
Income paid or payable, or otherwise made available in respect of the financial year to all executive officers, directly or indirectly by the		
company:	508,698	183,363
bands is:	2003 No.	2002 No.
	(a)	No.
\$10,000 - \$19,999	<u>-</u>	1
\$20,000 - \$29,999 \$60,000 - \$69,999	1	-
\$80,000 - \$89,999 \$80,000 - \$89,999	1 -	2
\$90,000 - \$99,999	1	-
\$160,000 - \$169,999	2	-

(a) Based on the method described in Note 16(a), total remuneration for the current financial year includes a value of \$399 for options granted to executives in the 2002 financial year, which had not vested at 1 July 2002. For further details see Note 16(a).

Details relating to options issued and the valuation basis adopted are as follows:

2,200,000 options were granted to officers during the 2002 financial year. Each option entitles the holder to purchase 1 ordinary share in Antisense Therapeutics Limited at an exercise price of 20 cents. These options were granted on 3 December 2001 on the same terms as those described in Note 16 (a) above, except that these options are not subject to any escrow arrangements.

The valuation of 0.00459 of a cent per option has been determined on the same basis as described in Note 16(a) above.

	2003 \$	2002 \$
NOTE 18. REMUNERATION OF AUDITORS		
Remuneration received, or due and receivable by the auditor for:		
Amounts received or due and receivable by Ernst &		
Young Australia for		
-an audit or review of the financial report of the entity	19,900	10,000
- other services in relation to the entity		
- tax compliance	15,152	-
- assurance related	1,500	•
Amounts received or due and receivable by auditors other		
than Ernst & Young for:		
- an audit or review of the financial report of the entity	-	3,500
- other services in relation to the entity		
- tax compliance	•	37,300
Total	36,552	50,800

		2003 \$	2002 \$
NOT	E 19. COMMITMENTS		yagang Waster
(a)	Expenditure commitments relating to research and develop	ment are payable as follows:	
Not la	ater than one year (i)	1,247,678	2,422,252
(i) (b)	This amount includes commitments relating to research and deventity on behalf of the company under a 3 year research agreeme research to be terminated with six months notice. Accordingly, company would be committed to in the event notice were to be a Lease Expenditure commitments:	ent, however, the agreement al the commitment reflects estim	lows for the
Not l	ater than one year	45,087	28,591
NOT	E 20. EMPLOYEE BENEFITS		
(a)	Employee benefits		
	Provisions (current) (Note 8)	38,101	15,415

## (b) Employee Option Ownership Scheme

Antisense Therapeutics Limited offers options over ordinary shares to employees at the discretion of the Board of Directors. There are currently five employees eligible to participate in this scheme. Options issued to employees are not listed options and as such do not have a readily available market value.

Details of the employee options ownership scheme are as follows:

	20	03	20	02
	Number of options	Weighted average exercise price	Number of options	Weighted average exercise price
Balance at beginning of year	5,350,000	0.20	•	-
- granted			5,350,000	0.20
- exercised		-	-	<u> </u>
Balance at end of year	5,350,000	0.20	5,350,000	0.20
Exercisable at end of year	1,070,000	0.20		-

The following summarises information about options held by employees as at 1 July 2002 and 30 June 2003 \*:

Number of Options	Grant Date	Vesting Dates	Expiry Date	Average Exercise Price
5,350,000	3 December 2001	1 August 2002 – 20% 1 August 2003 – 40% 1 August 2004 – 40%	31 July 2005	\$0.20

<sup>\*</sup> No options were granted during the year, and no options held by employees as at 1 July 2002 were exercised or expired during the year.

## NOTE 21. SUBSEQUENT EVENTS

On 20 August 2003, the company announced a placement of shares to Australian institutions and professional investors, raising \$5 million by the issue of 38.5 million shares at \$0.13 per share. As part of the placement, Polychip Pharmaceuticals Pty Limited (a wholly owned subsidiary of Circadian Technologies Limited) has agreed to subscribe for approximately \$1 million at \$0.13 per share. This is subject to shareholder approval which will be sought at the company's Annual General Meeting.

#### NOTE 22. SEGMENT INFORMATION

The company operates in one industry and one geographical segment, those being the pharmaceutical and healthcare industry and Australia respectively.

## **Directors' Declaration**

In accordance with a resolution of the directors of Antisense Therapeutic Limited, we state that:

- (1) In the opinion of the directors:
  - (a) the financial statements and notes of the company are in accordance with the Corporations Act 2001, including:
    - (i) giving a true and fair view of the company's financial position as at 30 June 2003 and of their performance for the year ended on that date; and
    - (ii) complying with Accounting Standards and Corporations Regulations 2001; and
  - (b) there are reasonable grounds to believe that the company will be able to pay its debts as and when they become due and payable.

On behalf of the Board

Robert W Moses Chairman

MANIN

Mark Paul Diamond
Managing Director

Melbourne 22 August 2003

## **OTHER INFORMATION**

2003 2002

NTA backing

Net tangible asset backing per ordinary security

\$0.03

\$0.04

#### **Ratios**

Net loss from ordinary activities after tax attributable to members as a percentage of equity at the end of the year

(52.6%)

(46.9%)

## Earnings per share

Basic earnings per share (cents per share) Diluted earnings per share (cents per share) (2.46)

(3.81)

(2.46)

(3.81)

#### Status of audit of accounts

This Appendix 4E is based on accounts which have been audited. The audit report is included with the financial report which forms part of this Appendix 4E.

## **Annual General Meeting**

The Annual General Meeting will be held as follows:

Place:

Rialto Towers

Level 23

525 Collins Street Melbourne, Victoria

Date:

31 October 2003

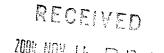
Time:

11.30am

Approximate date the annual report will be

available:

26 September 2003



CORPORATE FILLS Appendix 3B

Name of entity

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

Appendix 3B Page 1

## New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002, 1/1/2003.

Antisense Therapeutics Limited		
ough space).		
(ANP)		
ary shares.		

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	Yes
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A

5 Issue price or consideration

30,771,540 ordinary shares at \$0.13 cents per share

6 Purpose of the issue
(If issued as consideration for the acquisition of assets, clearly identify those assets)

Share placement to Australian institutions and professional investors issuing 30,771,540 shares at \$0.13 per share. The funds raised through the placement will be applied to the company's drug development projects: ATL1102 for multiple sclerosis, ATL1101 for psoriasis and other drug discovery activities.

7 Dates of entering \*securities into uncertificated holdings or despatch of certificates

25 August 2003

8 Number and \*class of all \*securities quoted on ASX (including the securities in clause 2 if applicable)

Number	+Class
172,740,640	Ordinary Shares (ANP)
91,469,665	Options (ANPO)
	ļ

Appendix 3B Page 2

<sup>+</sup> See chapter 19 for defined terms.

Number +Class 133,312,508 Number and +class of all Restricted ordinary shares \*securities not quoted on ASX (ANPAK) 11,500,000 (including the securities in clause Restricted options expiring 31 2 if applicable) July 2005 exercisable at 20 cents (ANPAM) 20,000,000 Restricted options expiring 30 November 2006 exercisable at 20 cents (ANPAO) 2,450,000 Options expiring 31 July 2005 exercisable at 20 cents (ANPAQ) 10 Dividend policy (in the case of a N/A trust, distribution policy) on the increased capital (interests) Part 2 - Bonus issue or pro rata issue 11 security holder approval N/A required? Is the issue renounceable or non-N/A12 renounceable? 13 Ratio in which the \*securities will N/A be offered 14 +Class of +securities to which the N/A offer relates +Record date determine N/A to entitlements 16 Will holdings on different registers (or subregisters) be aggregated for calculating entitlements? 17 Policy for deciding entitlements in relation to fractions Names of countries in which the entity has \*security holders who will not be sent new issue documents Note: Security holders must be told how their

entitlements are to be dealt with.

Cross reference: rule 7.7.

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

## Appendix 3B New issue announcement

19	Closing	date	for	receipt	of	N/A
	acceptant	ces or r	enunci	iations		

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a	N/A

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

<u>-</u> ,			
32	of the	do *security holders dispose ir entitlements (except by sale the broker)?	N/A
33	+Desp	atch date	N/A
		Quotation of secur	
34	Type (tick o	of securities one)	
(a)	<b>~</b>	Securities described in Part 1	
(b)		All other securities	
	Ш		of the escrowed period, partly paid securities that become fully paid, employee ends, securities issued on expiry or conversion of convertible securities
Ent	ities th	at have ticked box 34(a	a)
Add	itional s	ecurities forming a new cla	ss of securities
Tick docum		e you are providing the informa	tion or
35			securities, the names of the 20 largest holders of the number and percentage of additional *securities held by
36		*securities setting out the num	y securities, a distribution schedule of the additional aber of holders in the categories
		1 - 1,000 1,001 - 5,000	
		5,001 - 10,000 10,001 - 100,000	
		100,001 and over	
37		A copy of any trust deed for t	he additional *securities

Appendix 3B Page 6

<sup>+</sup> See chapter 19 for defined terms.

Entiti	ies that have ticked box 34(b)	l	
38	Number of securities for which function is sought		
39	Class of *securities for which quotation is sought		
40	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?		
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment		
41	Reason for request for quotation now  Example: In the case of restricted securities, end of restriction period		
	(if issued upon conversion of another security, clearly identify that other security)		
42	Number and *class of all *securities quoted on ASX (including the securities in clause 38)	Number	+Class

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

### Quotation agreement

- †Quotation of our additional \*securities is in ASX's absolute discretion. ASX may quote the \*securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

Appendix 3B Page 8

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before †quotation of the †securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

\_\_ \_ \_ \_ \_ \_

Sign here:

Natalie Korchev

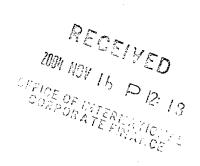
Date: 22 August 2003

Company secretary

Print name:

Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.



27 August 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

# Investor Update Re Multiple Sclerosis Compound - Initiation of Phase I Study

In line with a recent update provided in the Company's corporate presentation on 13 August 2003, Antisense Therapeutics yesterday commenced dosing of healthy volunteers in Phase I clinical studies of its multiple sclerosis product, ATL1102 at the Company's contracted clinical trial centre, Charterhouse Clinical Research Unit, Ravenscourt Park Hospital (formerly Stamford Hospital) in London. Antisense Therapeutics licensed ATL1102 from California-based Isis Pharmaceuticals Inc ('Isis') in 2001. ATL1102 is an exciting second-generation antisense compound, and our partner, Isis is to jointly announce with Antisense Therapeutics the initiation of this Phase I trial to the US market.

As announced by Antisense Therapeutics on 4 February 2003, this human trial is comprised of an evaluation of the safety and disposition (pharmacokinetics) of single escalating doses of ATL1102 given by injection to approximately 40 healthy volunteers. Antisense Therapeutics anticipates reporting the results of this trial by mid 2004. For further information refer to the Antisense Therapeutics/Isis joint announcement which follows.

Yours sincerely

Natalie Korchev Company Secretary

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999 Contact: Kristina Peterson
Isis Pharmaceuticals

760-603-2641

Natalie Korchev

Antisense Therapeutics Limited

+61 3 9827 8999

# ANTISENSE THERAPEUTICS LIMITED AND ISIS PHARMACEUTICALS INITIATE PHASE I TRIAL OF ANTISENSE DRUG FOR MULTIPLE SCLEROSIS

Melbourne, Australia and Carlsbad, CA, USA, August 27, 2003 – Antisense Therapeutics Limited (ASX:ANP) and Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today the initiation of a Phase I clinical trial of ATL1102 (ISIS 107248) for multiple sclerosis (MS). ATL1102 is an antisense inhibitor of VLA-4 (Very Late Antigen-4). Inhibition of VLA-4 has been shown to have positive effects in multiple animal models of inflammatory diseases, including MS. Isis licensed the compound to Antisense Therapeutics Ltd. ("ATL") in 2001.

"We are pleased to move ATL1102, our lead drug candidate, into the clinical setting," said Mark Diamond, Managing Director of ATL. "This trial is the first step in potentially improving the treatment of multiple sclerosis, which is a major unmet medical need. We are hopeful that this antisense drug, the first to be developed for multiple sclerosis, may provide patients with a new treatment option, as current therapies are limited."

The double-blinded, placebo controlled Phase I study will evaluate the pharmacokinetic and safety profile of ATL1102 in approximately 40 healthy volunteers. This trial is being conducted at the Charterhouse Clinical Research Unit of the Ravenscourt Park Hospital (formerly Stamford Hospital) in London.

"We are committed to the rapid advancement of Isis' proprietary second-generation antisense drugs. ATL1102 is our fourth second-generation compound to enter human clinical trials in the past 18-months," said Stanley T. Crook, M.D., Ph.D., Isis' Chairman and CEO. "This collaboration provides us with the opportunity to expand our pipeline through participation in the development of additional antisense drugs, while reducing expense and risk to Isis."

In December 2001, Isis and Circadian Technologies Limited (ASX: CIR), a leading Australian biotechnology commercialization firm, collaborated to create ATL. As part of the broad-based agreement, the companies established a five-year antisense drug discovery and development collaboration, which included Isis' license of ATL1102 to ATL. Isis manufactures drug for human clinical trials for ATL at ATL's cost. ATL is responsible for the clinical development and commercialization of the compound.

Isis' proprietary second-generation drugs are designed to provide greater potency, increased stability, enhanced oral bioavailability and the potential for decreased side effects for patients. These attributes, along with advances in formulations, expand the therapeutic scope of antisense technology.

According to the National Multiple Sclerosis Society, MS is an autoimmune disease that affects the central nervous system (CNS). Approximately 400,000 Americans acknowledge having MS, and every week about 200 individuals are diagnosed. Worldwide, MS may affect more than two million people.

Antisense Therapeutics Ltd. is an Australian publicly listed (ASX: ANP) biopharmaceutical drug discovery and development company. ATL's mission is to create, develop and commercialize novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ATL's access to these projects is derived from its technology and research collaborations with Isis Pharmaceuticals Inc. and the Murdoch Childrens Research Institute (MCRI). The MCRI, based at the Royal Children's Hospital in Melbourne, is a major Australian research institute with over 450 staff and operates as an independent non-profit organisation. California-based Isis is a world leader in the field of antisense drug technology. The collaboration agreement with Isis provides ATL with extensive access to Isis' antisense drug discovery technology of relevance to the treatment of viral, skin, growth and inflammatory disorders. ATL plans to commercialize its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ATL's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc., Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has commercialized its first product, Vitravene(R) (fomivirsen), to treat CMV-induced retinitis in AIDS patients. In addition, Isis has 11 antisense products in its development pipeline, with two in late-stage development and several in Phase II human clinical trials. Affinitak(TM) (formerly called LY900003 and ISIS 3521), an inhibitor of PKC-alpha, is in Phase III development for non-small cell lung cancer, and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is in Phase III clinical trials for Crohn's disease. Isis has a broad patent estate, as the owner or exclusive licensee of more than 1,200 issued patents worldwide. Isis' GeneTrove(TM) program uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services. The Ibis Therapeutics(TM) program is focused on the detection of infectious organisms and the discovery of small molecule drugs that bind to RNA. Additional information about Isis is available at www.isispharm.com.

## Page 3

This press release contains forward-looking statements about the potential of the investigational compound ATL1102 for multiple sclerosis, Isis Pharmaceuticals' collaboration with ATL and the potential of Isis' drug development programs. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and financing such activities. Actual results could differ materially from those projected in this release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail on Form 10-Q for the period ended June 30, 2003, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

Vitravene® is a registered trademark of Novartis AG.

GeneTrove<sup>™</sup> and Ibis Therapeutics<sup>™</sup> are trademarks of Isis Pharmaceuticals, Inc.

Affinitak™, a trademark of Eli Lilly and Company, is an investigational cancer compound being developed through an alliance between Lilly and Isis Pharmaceuticals, Inc. and marketed globally by Lilly.

###

2 September 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

#### Letter to Shareholders re Share Purchase Plan

Dear Shareholder

I am pleased to advise you that the directors of Antisense Therapeutics Limited ('Antisense') have established a share purchase plan ('Plan') to give existing shareholders the opportunity to purchase additional shares in Antisense.

Under the Plan your directors are offering shareholders the opportunity to purchase a maximum of \$5,000 worth of Antisense shares. Shares purchased under the Plan will not attract brokerage, stamp duty or any other transaction costs.

As you may be aware, Antisense recently raised additional capital of \$5 million for its drug development projects (including ATL1102 for multiple sclerosis and ATL1101 for psoriasis) by way of a private placement to 'exempt' professional investors. The Plan provides Antisense's other loyal investors with the opportunity to also participate in Antisense's equity raising programs without incurring any charges.

An offer is being made under the Plan to all shareholders, whose registered address is in Australia, who owned ordinary shares in Antisense at close of trade on 1 September 2003 including those shareholders who had purchased ordinary shares in Antisense in accordance with ASX Listing Rules by no later than the close of trade on that day. The offer is non-renounceable, which means that you cannot transfer your right to purchase shares under the offer to anyone else. Details of the offer are set out in the Offer and Acceptance Form and Terms and Conditions attached.

Applications must be made for a minimum of \$1,000 worth of shares, with multiples thereafter of \$1,000, up to a maximum of \$5,000 worth of shares. The shares will be issued at 13 cents per share which is the issue price paid by Australian institutions and professional investors in the Company's recent share placement.

The offer under the Plan has been structured to comply with ASIC Class Order 02/831. As such, the maximum application for \$5,000 worth of shares applies to all eligible shareholders even if they receive more than one offer from Antisense (for example, because they are a

joint holder of shares or because they hold more than one shareholding under separate share accounts). Antisense reserves the right to reject any application for shares where it believes this requirement has not been complied with.

The offer closes at 5.00 pm AEST on 1 October 2003 ('Closing Date'). To participate in the offer, you will need to return your completed Offer and Acceptance Form together with your cheque in Australian dollars for the full amount to which your acceptance relates so that it is received by Computershare Investor Services Pty Ltd (as detailed in the Offer and Acceptance Form) no later than 5.00 pm AEST on the Closing Date. Applications received after the Closing Date will not be accepted.

It is expected that shares issued under the Plan will be quoted on Australian Stock Exchange on or about 13 October 2003 and you should receive your holding statement shortly after this date.

In deciding whether to take up the enclosed offer of shares, you should seek your own independent financial, legal and taxation advice in respect of the offer.

If you have any questions in relation to the Plan, please contact the Company's share registry, Computershare Investor Services Pty Limited on 1300 850 505 or + 61 3 9615 5970.

Yours sincerely

Robert Moses Chairman

Antisense Therapeutics Limited

ANTISENSE THERAPEUTICS LIMITED ABN 41 095 060 945 SHARE PURCHASE PLAN ("PLAN") APPLICATION FORM

All registry communications to: c/- Computershare Investor Services Pty Ltd GPO Box 52 Melbourne, Victoria 8060

Enquiries (within Australia) 1300 850 505 (outside Australia) 61 3 9615 5970 Facsimile 61 3 9473 2529 web.queries@computershare.com.au www.computershare.com

Shareholder Name & Address:

Record Date: 4 September 2003 Opening Date: 10 September 2003

1 October 2003

Closing Date: Issue Date:

8 October 2003

**BAR CODE** 

10000000000 

## A APPLICATION

I/We, the above shareholder(s), being registered as ordinary shareholder(s) in the Company as at the Record Date for this offer do hereby apply for new shares as indicated below at an issue price calculated in accordance with the Terms and Conditions of the Antisense Therapeutics Limited Share Purchase Plan, as attached and as otherwise set out in the accompanying letter dated 5 September 2003.

Applications must be made for a minimum of \$1,000 worth of shares, with multiples of \$1,000 thereafter, up to a maximum of \$5,000 worth of shares.

Please tick the a	appropriate box				
	\$1,000	\$2,000	\$3,000	\$4,000	\$5,000
B PAYME	NT DETAILS		and the second		

Drawer	BSB	Amount
		A\$

### C CERTIFICATION

For the purpose of the ASIC Class Order 02/831, you certify and confirm that the aggregate price for:

- (a) shares you have applied for under this application; and
- any other shares you have applied for under this Plan or any other Company share purchase plan or similar arrangement in the 12 months prior to the date of your application, (including through joint and/or beneficial holdings) does not exceed \$5,000.

Signature(s): Date:

- If you want to participate in this offer, please carefully read the Terms and Conditions of the offer attached.
- Complete all the required details on the Application Form, noting that all amounts are expressed in Australian Dollars. 2.
- Write the cheque for the exact amount of the Shares you want to acquire. Please make the cheque payable to Antisense 3. Therapeutics Limited.
- 4. Please return the Application Form, together with the cheque, to Computershare Investor Services Pty Limited, GPO Box 52, Melbourne, Victoria 8060.
- 5. Ensure that your Application Form and cheque reach us by the closing date of the offer being no later than AEST 5 pm on 1 October 2003.
- If signed under power of attorney, the attorney states that they have not received a notice of revocation of that power.

By accepting this offer you agree to be bound by the Terms and Conditions of the Offer and the Constitution of the Company.

# ANTISENSE THERAPEUTICS LIMITED SHARE PURCHASE PLAN

Pursuant to the Antisense Therapeutics Limited Share Purchase Plan ("Plan"), Antisense Therapeutics Limited ABN 41 095 060 745 ("Antisense") offers eligible shareholders the ability to apply for a minimum of \$1,000 and a maximum of \$5,000 worth of fully paid ordinary shares ("Shares") in Antisense ("Offer").

If you are eligible to apply for Shares, you may apply for a minimum of \$1,000 worth of Shares and in multiples of \$1,000 thereafter, up to a maximum of \$5,000 worth of Shares.

Please carefully read the Terms and Conditions relating to the Offer as you will be bound by them. By lodging this form with your cheque, you confirm that you have read, understood and agreed to the terms and conditions of the Plan.

#### TERMS AND CONDITIONS

#### 1. Participation

Participation in the Plan is open to all persons who, as at the record date determined by the directors of Antisense ('Board'), are registered as holders of ordinary shares in Antisense, except those shareholders whose registered address is in a country where, in the reasonable opinion of the Board, it is unlawful or impractical for Antisense to issue offers under the Plan.

Participation in the Plan is optional and is subject to these terms and conditions.

#### 2. Offers

Offers under the Plan will be non-renounceable and shares may be issued only to the shareholder to whom they are offered

Each offer will be made on the same terms and conditions. All eligible shareholders of Antisense will receive the same offer, irrespective of the number of shares which they hold on the record date.

Offers to subscribe for shares under the Plan may be made once a year, or as otherwise determined by the Board. In any consecutive 12 month period, the maximum value of shares for which each eligible shareholder may subscribe under the Plan is \$5,000 (or such lesser amount as the Board may determine in its discretion). This limit applies to each shareholder even if that person holds shares in more than one capacity – for example, as a sole holder and as a first (or subsequent) named holder of two or more joint holders. However, a trustee or nominee expressly noted on a company register may receive an offer for each occasion they are separately recorded as a trustee or nominee for a different beneficiary named on that register.

Offers will be made subject to any terms and conditions that the Board thinks fit which are consistent with these terms and conditions, including any minimum subscription amount. The Board may also determine the multiple(s) of shares, or the fixed dollar amount(s), for which each eligible shareholder may subscribe under any given offer under the Plan.

## 3. Issue Price

Shares will be issued under the Plan at the issue price determined by the Board, which must be less than the market price during a specified period in the 30 days prior to either the date of the offer or the date of issue of shares under the offer.

#### 4. Costs of Participation

No brokerage, commissions, stamp duty or other transaction costs will be payable by shareholders in respect of the application for, and issue of, shares under the Plan.

#### 5. Issue of Shares

Antisense will issue shares for the purposes of an offer as soon as reasonably practicable after the closing date of the relevant offer.

Shares issued under the Plan will rank equally with all other ordinary shares in Antisense on issue as of the date of issue and will therefore carry the same voting rights, dividend rights and other entitlements as those shares.

Antisense will apply for shares issued under the Plan to be quoted on Australian Stock Exchange Limited ('ASX').

Antisense will, within the period required by the ASX Listing Rules, send participants a holding statement in respect of any shares issued to them under the Plan.

#### 6. Acceptance of Offers

An offer to participate in the Plan may be accepted by an eligible shareholder only by completing and returning the acceptance form provided by Antisense, together with the appropriate payment for the amount to which the acceptance relates, by no later than the closing date for the offer specified on the acceptance form.

Payment may be made only by cheque in Australian dollars drawn on an Australian bank.

An offer will be taken to have been accepted by an eligible shareholder only if the cheque which accompanies the shareholder's acceptance form is paid in full on first presentation.

If one or more acceptance forms are received by an eligible shareholder in relation to shares with a value greater than \$5,000 in any consecutive 12 month period, the shareholder will be issued with the maximum number of shares permitted by the Plan and the excess subscription monies will be refunded (without interest).

If an eligible shareholder subscribes for an amount which is not exactly divisible by the issue price for the shares, in calculating the number of shares to be issued, all fractional entitlements will be rounded up to the nearest whole number.

#### 7. Amendment, Suspension and Termination of the Plan

The Board may, in its discretion, amend, suspend or terminate the Plan at any time and adopt any administrative procedures it thinks appropriate in relation to the Plan. Antisense may issue to any person fewer shares than subscribed for under the Plan (or none at all) if Antisense believes that the issue and allotment of those shares would contravene any law or the rules of any stock exchange on which Antisense shares are quoted.

### 8. Dispute Resolution

Antisense may settle, in any manner it thinks fit, any difficulties, anomalies or disputes which may arise under or in connection with the operation of the Plan, whether generally or in relation to any participant or class of participants, offer, application or shares, and the decision of Antisense shall be conclusive and binding on all participants and other persons to whom the determination relates.

Antisense reserves the right to waive compliance with any provision of these terms and conditions.

## 9. Notices

Notices and statements to participating shareholders may be given in any manner determined by the Board from time to time.

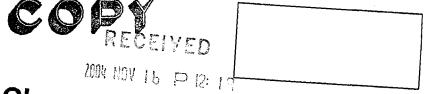
#### 10. Privacy

Chapter 2C of the Corporations Act 2001 requires information about shareholders (including name, address and details of the shares held) to be included in Antisense's public register. If a shareholder ceases to be a shareholder, Chapter 2C of the Corporations Act 2001 requires this information to be retained in Antisense's public register. These statutory obligations are not altered by the Privacy Act 1988 (Cth) as amended. Information is collected to administer shareholders' security holdings.



ASIC

Australian Securities & Investments Commission



# Change to company details

Form 484 — Corporations Act 2001

# Section C

Section C may be lodged independently if no changes are to be notified via Sections A or B.

Use this form to notify ASIC of:

- C1 Change to share structure table
- C2 Issue of shares
- C3 Cancellation of shares
- C4 Changes to members' register

## Related Forms

484 A - change of address, name (officeholders or members), details (ultimate holding company)
484 B - appoint/cease officeholder, change special purpose company status

If there is insufficient space in any section of the form, you may photocopy the relevant page(s) and submit as part of this lodgement

# Company details

	- ioagoment	•
Company name		
ANTISENSE TH	EPA DEUE	
ACN/ABN	ERAPEUTICS LIMITED	
41 095 060		
77.060	745	
Is this document being lodged to	o update the Annual Company Statement that was sent to	
Yes	Satement that was sent to	you?
X No		
_		_

# Section C completion guide

## Standard share codes

Refer to the following table for the share class codes for sections C1, C2, C3 and C4

Share c code	lass Full title	Share class code	Ful) title
A B	A	PRF	preference
EMP	Betc employee's	CUMP	cumulative preference
Fou	founder's	NCP REDP	non-cumulative preference
.G	life governor's	INRP	redeemable preference
MAN ORD	management		non-redeemable preference
ED	ordinary	NCRP	cumulative redeemable preference non-cumulative redeemable preference
PE	redeemable special	PARP	participative preference

Continues on next page...

ASIC Form 484 Section C 1 July 2003

If you are using the standard share class codes you do not need to provide a full title for the shares.

If you are not using the standard share class code, enter a code of no more than 4 letters and then

## Sections to complete

Use the table below to identify the sections of this form to complete (please indicate the sections that have been completed). Completion of this table is optional.

	C1 - Change to share structure table	C2 - Issue of shares	C3 - Cancellation of shares	C4 - Change to members register
Issue of shares				
Proprietary company			Not required	1
Public company				
if in response to the Annual company statement	<b>/</b>		Not required:	1
if not in response to the Annual company statement	Not required		Not required	Not required
Cancellation of shares				
Proprietary company	<b>V</b>	Not required		
Public company				
If in response to the Annual company statement	<b>/</b>	Not required	/	7
if not in response to the Annual company statement.	Not required:	Not required		Not required
Transfer of shares				
Proprietary company	Not required	Not required	Not required	
Public company				
if in response to the Annual company statement	Not required	Not required	Not required	
if not in response to the Annual company statement	Not required	Not required	Not required	Not required
Changes to amounts paid				
Proprietary company	7	Not required	Not required	/
Public company				
if in response to the Annual company statement		Not required	Not required	
if not in response to the Annual company statement	Not required	Not required	Not required	Not required
Changes to beneficial ownership				
Proprietary company	Not required	Not required	Not required	/
Public company				
if in response to the Annual company statement	Not required	Not required	Not required	
if not in response to the Annual company statement	Not required	Not required	Not required	Not required

To notify ASIC about a division or conversion of a class of shares, you must lodge a form 211.

To notify ASIC about a conversion of shares into larger or smaller numbers, you must lodge a form 2205.

C1 Cha	nge to	share	structure	table
--------	--------	-------	-----------	-------

Where the share class has changed (eg. as a result of the issue or cancellation or shares), please show the updated details for this share class in the table below. Details of share classes that have not changed are not required here.

Share class code	Full title if not standard	Total number issued	Total amount paid on these shares	Total amount unpaid on these shares
		· · · · · · · · · · · · · · · · · · ·		
				N. C
				Fig.
liest date of chang				
se indicate the earli	est date that any of the above changes occured			
. Dj. [M . M	η [ <del>Υ.   Υ</del> ] ,			

## C2 issue of shares

List details of new share issues in the following table.

	Number of shares issued	Amount paid per share	Amount unpaid per share
ORD	30,771,540	\$0.13	NIL
ORD	900	\$0.20	NIL
ease indicate the earl	gel lest date that any of the above changes B / 0 3 /] [Y Y]	occured The state of the state	
esse indicate the earl 2 5 / 0 8 D) [M h	est date that any of the above changes    / 0 3    /	occured  all of the shares issued under a written a	contract?
2 5 10 E	est date that any of the above changes    / 0 3    /		

## C3 Cancellation of shares

Reason for cancellation Please indicate the reason that shares have been cancelled (select one or more boxes)	Redeemable preference shares — \$.254J  Redeemed out of proceeds of a fresh issue of shares  Capital reduction — \$.256A - \$.256E  Single shareholder company Multiple shareholder company: A Form 2560 must be lodged before a capital.			
	reduction takes place  Share buy-back — ss.257H(3)  Minimum holding buy-back only  Other buy-back type. A form 280 or 281 must be lodged at least 14 days, and no more than 1 year before the share buy-back can take place			
	Forfeited shares — \$.258D  Shares returned to a public company — ss.258E(2) & (3)  Under section 651C, 724(2), 737 or 738  Under section 1325A (court order)  Other  Description			
Details of cancelled shares	Give section reference:  List the details of shares cancelled in the following table			
- The state of the	Share class code Number of shares cancelled Amount paid (cash or otherwise)			
	Earliest date of change  Please Indicate the earliest date that any of the above changes occured			

## C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B).
- If shares are jointly owned, provide names and addresses of all joint owners on a separate sheet, clearly indicating the share class and with whom the shares are jointly owned.

Please complete a separate section below for each member

The changes apply to Please indicate the name and address of the member whose shareholding has changed		has	Family name OR Company na ACN/ARBN Office; unit, level,	ume V/ABN or PO Box numb	er	Given n	ames		
			Suburb/City  Postcode	Country (if no	t Australia)	Sta	ate/Territory		
The changes  Share class.  Code	Shares increased by (number)	Shares decreased by (number)	Numbernow	Total \$ paid on these shares	Total \$ unpaid on these shares	Fully paid (V/n)	Beneficially held (y/n)	Top.20 member (y/n)	
Earliest date of Please indicate the of the above change Date of entry of register	e earliest date that ges occurred member's nar	nt any	Date Date Date DD D						
(New members on	ry) ection C 1 July 20(		[D   D]   M					Page Stof	

## C4 Continued... Further changes to the register of members

The changes apply to Please indicate the name and address of the member whose shareholding has changed	Family name Given names .	
	Company name  ACN/ ARBN/ ABN  Office, unit, level, or PO Box number	
	Street number and Street name  Suburb/City State/Territory Postcode Country (if not Australia)	
The changes are  Share class Shares Share code increased by decre (number) (n	Number now Total \$ paid Total \$ Fully paid Beneficially Top 20 held on these unpaid (y/n) held (y/n) member (y/n) on these shares	
Earliest date of change Please indicate the earliest date that any of the above changes occurred		
Date of entry of member's name in register (New members only)		
ASIC Form 484 Section C 1 July 2003		3

## C4 Continued... Further changes to the register of members

The changes apply to Please indicate the name and address of the member whose shareholding has changed	Family name Gryen names  OR	
	Company name	
	AGN/ARBN/ABN	
	Office, unit, level, or PO Box number  Street number and Street name	
	Suburb/City. State/Territory	
	Postcode Country (if not Australia)	
The changes are  Share class Shares Shares code increased by decrea (number)(number)	Number now Total \$ paid Total \$ Fully paid Beneficially Top 20 seed by held on these unpaid (y/n) held (y/n) shares on these shares	
Earliest date of change Please indicate the earliest date that any of the above changes occurred		
Date of entry of member's name in register (New members only)	Date  Date  D   M M M   Y Y	
ASIC Form 484 Section C 1 July 2003	Page 7:01	9

## C4 Continued... Further changes to the register of members

The changes apply to Please indicate the name and address of the member whose shareholding has changed	Family name Given names
Changed	OR Company name:
	ACN/ARBN/ABN  Office, unit, level, or PO Box number
	Street number and Street name
	Suburb/City State/Territory.
Talifornia, p. green and proping	Postcode Country (if not Australia)
Share class Shares Share Code Increased by decreased by decrease	Number now Total \$ paid Total \$ Fully paid Beneficially Top 20 held on these unpaid (y/n) member
· · · · · · · · · · · · · · · · · · ·	
ASIC Form 484 Section C 1 July 2003	Page 8.of 9

## Signature

This form must be signed by a current officeholder of the company.

NATALIE KORCHE	V			
apacity				
Director				
X Company secretary				
ignature			A 167, 173, 163 -170 ( 1104)	
N. Korchev				
ate signed				
1   9   1   0     9   1   0   3				

## Lodging party details

Please notify the registered agent details (if applicable) and to whom queries about this form should be directed.

## Registered Agent details

If this form is being lodged by an ASIC registered agent, please complete agent name and number

## Queries about this form

You can nominate an officeholder, lodging party or ASIC registered agent

SIC	registered agent number	
ane		
the	ere is a query regarding this form, ASIC should contact (Choose one of the following)	
x	Signatory above	
	ASIC registered agent above	
	Acic registered agent above	
<u>×</u> ]	Name of lodging party	
	ANTISENSE THERAPEUTICS LIMITED	
	Office, unit, level, or PO Box number	
	LEVEL 1	
	Street number and Street name	
	10 WALLACE AVENUE	
	Suburb/City State/Territory TOORAK L VTC	
	Postcode Country (if not Australia)	7
	DX Number DX City/suburb	
	DX Number DX City/suburb	1
	Telephone Number	
	03 9827 8999	



Mail

Send completed and signed forms to: Australian Securities and Investments Commission, PO Box 4000, Gippsland Mail Centre VIC 3841. For help or more information

Telephone

03 5177 3988

Email

info.enquiries@asic.gov.au

Web

www.asic.gov.au/easylodge

lodging party or agent name office, level, building name or PO Box no.	ANTISENSE THERAPEUTICS LIMITED LEVEL 1	BY
street number & name	10 WALLACE AVENUE DECEMEN	
suburb/city	TOORAK state/territory VIC postcode 3142	
telephone	(02) 0007 0000	7 455 57 850 4 57
facsimile	(03 ) 9827 1166 2004 NOV 16 P 12 1	ASS. REQ-A REQ-P
DX number	suburb/city	PROC.
	COMPONATE FIRE CO.	
	Australian Securities & Investments Commission form 388	
	Corporations Act 200	1
	copy of financial statements and reports 294, 295, 298-300, 307	
	Corporations Regulation	
	1.0.08	j
Name	ANTISENSE THERAPEUTICS LIMITED	
ACN / ARBN / ARSN/PIN	41 095 060 745	
	11 000 000 745	
Reason for lodgement of	of statements and reports	j
tick the appropriate box		(A)
•	A registered scheme*	(B)
	Amendment of financial statements or directors' report (company)	(C)
	Amendment of financial statements or directors' report (registered scheme)*	(D)
	☐ A large proprietary company that is not a disclosing entity	(H)
	A small proprietary company that is controlled by a foreign company for all or part of the period and where the	
	company's profit or loss for the period is not covered by the statements lodged with ASIC by a registered foreign	w
	company, company, registered scheme, or disclosing entity	(1)
	A small proprietary company that is requested by ASIC to prepare and lodge statements and reports	(J)
	A prescribed interest undertaking that is a disclosing entity	(K)
Dates on which financial year begins Date of Annual General Meeting (if ap	1 / 7 / 2002 and ends 30 / 6 / 2003 plicable) 31 / 10 / 2003	(d/m/y)
Details of large proprie		
	If the company is a large proprietary company that is not a disclosing entity, please complete the following information of the financial year for which the financial statements relate:	on as at the
A	What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?	•
8	What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?	
C	How many employees are employed by the large proprietary company and the entities that it controls?	
	How many members does the large proprietary company have?	
	•	
Auditor report		
Additor report	·	
Were the financial statements au	dited? Yes ፟ No □	
	: Does the auditor's report (section 308) for the financial year contain a statement of:	
ii yes	* reasons for the auditor not being satisfied as to the matters referred to in section 30?? Yes	No ☑
	* details of the deficiency, failure or shortcoming concerning any matter referred to in section 307? Yes	No 🔀
If no	: Is there a class order exemption current for audit relief?	No 🗌
***************************************	100 L	<b>-</b>
• NOTE	: Where a new auditor has been appointed to a Registered Scheme, Form 5137 - Appointment of Scheme Auditor	r must be lodged

<b>Details of current audito</b>	r*		
•	The auditor can be a person or a firm.		
lf a person			
name (family & given names)			
Auditor Registration no:		· · · · · · · · · · · · · · · · · · ·	
-	office	level	building name
street number & name			
suburb / city		state / territory	postcode
date of appointment (d/m/y)	1 1		
_			
OF			•
lf a firm			
name of firm	ERNST & YOUNG		
	office	level 23	building name
	120 COLLINS STREET		
suburb / city	MELBOURNE	state / territory VIC	postcode 3000
Business Registration number	(if applicable) 0.9 2154 9U	Stat	e / Territory registered in VTCTORTA
date of appointment (d/m/y)	9 / 7 / 2002		
Statements and reports	to be attached to this form		
•	•		
`	Financial statements for the year (as per ss29	5(2))	
	statement of financial performance for the year	ar (profit and loss statement)	
	statement of financial position as at the end of	of the year (balance sheet)	
statement of cash flows for the year			
•	if required by accounting standards - consolid	lated profit & loss statement, b	alance sheet and statement of cash flows
	Notes to financial statements (as per ss295(3)	))	
	disclosures required by the regulations		
	notes required by the accounting standards		
	any other information necessary to give a true	e and fair view (see s297)	
	The directors' declaration about the statement	its and notes (as per ss 295(4))	
	The directors' report for the year (as per s 298	8 to 300)	
	Auditor's report required under sections 308	and 314	
	1		
Certification			
	I certify that the attached documents marked	( ) are a true copy of the	annual reports required under Section 319.
	NATALIE KORCHEV	,	COMPANY SECRETARY
print name		ca	pacity
-: b	N/ W. Jay		19/9/2003
sign here	2 4. Sevenor	da	te 19/9/2009
			,
			I and the second
	NAME OF THE PARTY	B 1. 10. = =	
NOTE:	Where a new auditor has been appointed to	a Registered Scheme, Form 5	137 - Appointment of Scheme Auditor must be lodged
			•
	<u> </u>	·	
	Small Business (less than 20 employees), plo	ease provide an estimate of the	time taken to complete this form
	Include		
			estion and obtaining the information
	The time spent by all employees in		

hrs

mins

7000 1137 16 P 12: 17

CEFICE OF INTERPORTED CONFORATE FINANCE

Name of entity

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

# **Appendix 3B**

# New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002, 1/1/2003.

Antis	sense Therapeutics Limited	
ABN 41 09	95 060 745	
We (	the entity) give ASX the following i	nformation.
	t 1 - All issues ust complete the relevant sections (attach si	heets if there is not enough space).
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	Ordinary Shares (ANP)
2	Number of *securities issued or to be issued (if known) or maximum number which may be issued	900
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	Fully paid ordinary shares.

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	Yes	
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
5	Issue price or consideration	900 ordinary shares at \$6	0.20 cents per share
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)		to purchase 900 shares (originally issued on 26 opiring on 1 February
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	25 August 2003	
8	Number and <sup>†</sup> class of all <sup>†</sup> securities quoted on ASX ( <i>including</i> the securities in clause	Number 172,741,540 91,468,765	+Class Ordinary Shares (ANP) Options (ANPO)
	2 if applicable)		

Appendix 3B Page 2

<sup>+</sup> See chapter 19 for defined terms.

Number +Class 133,312,508 Number and +class of all Restricted ordinary shares +securities not quoted on ASX (ANPAK) (including the securities in clause 11,500,000 Restricted options expiring 31 2 if applicable) July 2005 exercisable at 20 cents (ANPAM) 20,000,000 Restricted options expiring 30 November 2006 exercisable at 20 cents (ANPAO) 2,450,000 Options expiring 31 July 2005 exercisable at 20 cents (ANPAQ) 10 Dividend policy (in the case of a N/A trust, distribution policy) on the increased capital (interests)

## Part 2 - Bonus issue or pro rata issue

	P	
11	Is security holder approval required?	N/A
12	Is the issue renounceable or non-renounceable?	N/A
13	Ratio in which the *securities will be offered	N/A
14	<sup>+</sup> Class of <sup>+</sup> securities to which the offer relates	N/A
15	<sup>+</sup> Record date to determine entitlements	N/A
16	Will holdings on different registers (or subregisters) be aggregated for calculating entitlements?	N/A
17	Policy for deciding entitlements in relation to fractions	N/A
18	Names of countries in which the entity has *security holders who will not be sent new issue documents	N/A
	Note: Security holders must be told how their entitlements are to be dealt with.	
	Cross reference: rule 7.7.	

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

19 Closing date for receipt of N/A acceptances or renunciations

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a	N/A

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

32	How do *security holders dispose of their entitlements (except by sale	N/A
	through a broker)?	
33	<sup>+</sup> Despatch date	N/A
Par	t 3 - Quotation of secur	ities
ou ne	ed only complete this section if you are app	lying for quotation of securities
34	Type of securities (tick one)	
(a)	Securities described in Part 1	
(b)	All other securities	
	Example: restricted securities at the end	of the escrowed period, partly paid securities that become fully paid, empl-
		ends, securities issued on expiry or conversion of convertible securities
Enti		ends, securities issued on expiry or conversion of convertible securities
	incentive share securities when restriction	ends, securities issued on expiry or conversion of convertible securities
	incentive share securities when restriction ties that have ticked box 34(a	ends, securities issued on expiry or conversion of convertible securities
Addi	ties that have ticked box 34(ational securities forming a new classic indicate you are providing the information	ands, securities issued on expiry or conversion of convertible securities  a)  ass of securities
<b>Addi</b> Tick te	ties that have ticked box 34(ational securities forming a new classic indicate you are providing the informations.  If the *securities are *equity*	a)  ass of securities  tion or  securities, the names of the 20 largest holders of
<b>Addi</b> Tick to docum	incentive share securities when restriction  ties that have ticked box 34(a  tional securities forming a new cla  o indicate you are providing the informatents  If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity additional *equity additi	a)  ass of securities  tion or  securities, the names of the 20 largest holders of number and percentage of additional *securities held
Addi Tick to docum 35	incentive share securities when restriction  ties that have ticked box 34(a  tional securities forming a new cla  providing the information indicate you are provided in the informat	a)  ass of securities  tion or  securities, the names of the 20 largest holders of number and percentage of additional *securities held  y securities, a distribution schedule of the addition
Addi Tick to docum 35	incentive share securities when restriction  ties that have ticked box 34(a  tional securities forming a new cla  or indicate you are providing the information  If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity additional *securities are *equity additional *securities are *equity additional *securities are *equity *securities setting out the num 1 - 1,000  1,001 - 5,000  5,001 - 10,000	a)  ass of securities  tion or  securities, the names of the 20 largest holders of number and percentage of additional *securities held  y securities, a distribution schedule of the addition
Addi Tick to docum 35	incentive share securities when restriction  ties that have ticked box 34(a  tional securities forming a new cla  or indicate you are providing the information  If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity additional *securities are *equity additional *securities are *equity additional *securities are *equity *securities setting out the num 1 - 1,000 1,001 - 5,000	a)  ass of securities  tion or  securities, the names of the 20 largest holders of number and percentage of additional *securities held  y securities, a distribution schedule of the addition
Addi Tick to docum 35	incentive share securities when restriction  ties that have ticked box 34(a  tional securities forming a new cla  principal indicate you are providing the information indicate you are provided the information indicate you are providing the	a)  ass of securities  tion or  securities, the names of the 20 largest holders of a number and percentage of additional *securities held  y securities, a distribution schedule of the additional of holders in the categories
Addi Tick to docum 35	incentive share securities when restriction  ties that have ticked box 34(a  tional securities forming a new cla  or indicate you are providing the informations  If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity *securities setting out the num  1 - 1,000  1,001 - 5,000  5,001 - 10,000  10,001 - 100,000  100,001 and over	a)  ass of securities  tion or  securities, the names of the 20 largest holders of a number and percentage of additional *securities held  y securities, a distribution schedule of the additional of holders in the categories
Addi Tick to docum 35	incentive share securities when restriction  ties that have ticked box 34(a  tional securities forming a new cla  or indicate you are providing the informations  If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity *securities setting out the num  1 - 1,000  1,001 - 5,000  5,001 - 10,000  10,001 - 100,000  100,001 and over	a)  ass of securities  tion or  securities, the names of the 20 largest holders of a number and percentage of additional *securities held  y securities, a distribution schedule of the additional of holders in the categories

<sup>+</sup> See chapter 19 for defined terms.

Entities that have ticked box 34(b)						
38	Number of securities for which quotation is sought					
39	Class of *securities for which quotation is sought					
40	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?					
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment					
41	Reason for request for quotation now  Example: In the case of restricted securities, end of restriction period					
	(if issued upon conversion of another security, clearly identify that other security)					
42	Number and *class of all *securities quoted on ASX (including the securities in clause 38)	Number	+Class			

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

## Quotation agreement

- <sup>†</sup>Quotation of our additional <sup>†</sup>securities is in ASX's absolute discretion. ASX may quote the <sup>†</sup>securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

Appendix 3B Page 8 1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before †quotation of the †securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here:

Natalie Korchev

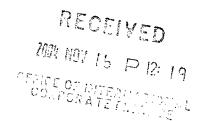
Date: 22 September 2003

Company secretary

Print name:

Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.



8 October 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Share Purchase Plan - Raises \$5.4 million

Cash Reserves of \$15.4 million, no borrowings

Antisense Therapeutics Limited (ASX: ANP) is pleased to advise that the company has received applications for a total of 41,508,302 shares at \$0.13 per share, raising \$5.4 million under its share purchase plan offer to eligible shareholders of the company (details of this offer were announced on 2 September 2003). The Directors believe that this is an exceptional result with almost half of all eligible shareholders participating in the offer. These shares have been allotted today.

The funds raised through the placement will be applied to further progress Antisense Therapeutics' drug development projects: ATL1102 for multiple sclerosis, ATL1101 for psoriasis and other drug discovery activities.

The company's cash reserves after its recent private placement to Australian institutions and professional investors and the funds received pursuant to the share purchase plan amount to \$15.4 million. This cash balance excludes the \$1 million subscribed for by Circadian Technologies Limited in the private placement, which is subject to shareholder approval at the company's Annual General Meeting on 31 October 2003.

The Directors of the company would like to thank Antisense Therapeutics' shareholders for their strong show of support through this offer.

An Appendix 3B requesting quotation of the 41,508,302 shares allotted today and of 1,000 shares purchased through the exercise of options is enclosed.

Yours sincerely

Natalie Korchev Company Secretary

#### About Antisense Therapeutics Limited

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Further company details are available on the Antisense Therapeutics website.

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

# Appendix 3B

## New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and

docun	nents given to ASX become ASX's property a	ınd ma	ry be made public.
Introdu	ced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/9	9, 1/7/2	000, 30/9/2001, 11/3/2002, 1/1/2003.
	of entity		
Anti	sense Therapeutics Limited		
ABN			
41 0	95 060 745		
	(the entity) give ASX the following i	nforr	nation.
	nust complete the relevant sections (attach si	heets ij	f there is not enough space).
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	Ord	inary Shares (ANP)
2	Number of *securities issued or to be issued (if known) or maximum number which may be issued		41,508,302 1,000
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	2.	Issue of 41,508,302 ordinary shares subscribed to by existing shareholders at \$0.13 per share pursuant to the company's share purchase plan (the terms of the share purchase plan were announced on 2 September 2003).  Exercise of 1,000 ANPO options at \$0.20 each.
		i .	

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	Yes	
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
5	Issue price or consideration	Subscriber monies of share – Total \$5,396,6     1,000 ordinary share share.	
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	Issue of 41,508,302 s existing shareholder company's share pure     Exercise of 1,000 AN	rs pursuant to the chase plan.
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	<ol> <li>8 October 2003</li> <li>24 September 2003</li> </ol>	
8	Number and *class of all *securities quoted on ASX (including the securities in clause 2 if applicable)	214,250,842	*Class Ordinary Shares (ANP) Options (ANPO)

Appendix 3B Page 2

<sup>+</sup> See chapter 19 for defined terms.

+Class

Number and +class of all 133,312,508 Restricted ordinary shares +securities not quoted on ASX (ANPAK) (including the securities in clause 11,500,000 Restricted options expiring 31 2 if applicable) July 2005 exercisable at 20 cents (ANPAM) 20,000,000 Restricted options expiring 30 November 2006 exercisable at 20 cents (ANPAO) Options expiring 31 July 2,450,000 2005 exercisable at 20 cents (ANPAQ) Dividend policy (in the case of a trust, distribution policy) on the increased capital (interests) Part 2 - Bonus issue or pro rata issue 11 security holder approval N/A required? 12 Is the issue renounceable or non- N/A renounceable? 13 Ratio in which the \*securities will N/A be offered 14 \*Class of \*securities to which the N/A offer relates 15 \*Record date determine N/A to entitlements 16 Will holdings on different registers N/A (or subregisters) be aggregated for calculating entitlements? Policy for deciding entitlements in N/A 17 relation to fractions Names of countries in which the N/A entity has \*security holders who will not be sent new issue documents Note: Security holders must be told how their entitlements are to be dealt with. Cross reference: rule 7.7. 19 Closing date for receipt of N/A acceptances or renunciations

Number

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a	

Appendix 3B Page 4

<sup>+</sup> See chapter 19 for defined terms.

32	How do *security holders dispose of their entitlements (except by sale through a broker)?	N/A			
33	<sup>+</sup> Despatch date	N/A			
	t 3 - Quotation of secur				
34	Type of securities (tick one)				
(a)	Securities described in Part 1				
(b)	(b) All other securities  Example: restricted securities at the end of the escrowed period, partly paid securities that become fully paid, employee incentive share securities when restriction ends, securities issued on expiry or conversion of convertible securities				
Enti	ties that have ticked box 34(a	a)			
Addi	tional securities forming a new cla	ss of securities			
Tick to docum	o indicate you are providing the informa ents	tion or			
35		securities, the names of the 20 largest holders of the number and percentage of additional *securities held by			
36		y securities, a distribution schedule of the additional aber of holders in the categories			
	10,001 - 100,000 100,001 and over				
37	A copy of any trust deed for t	he additional *securities			

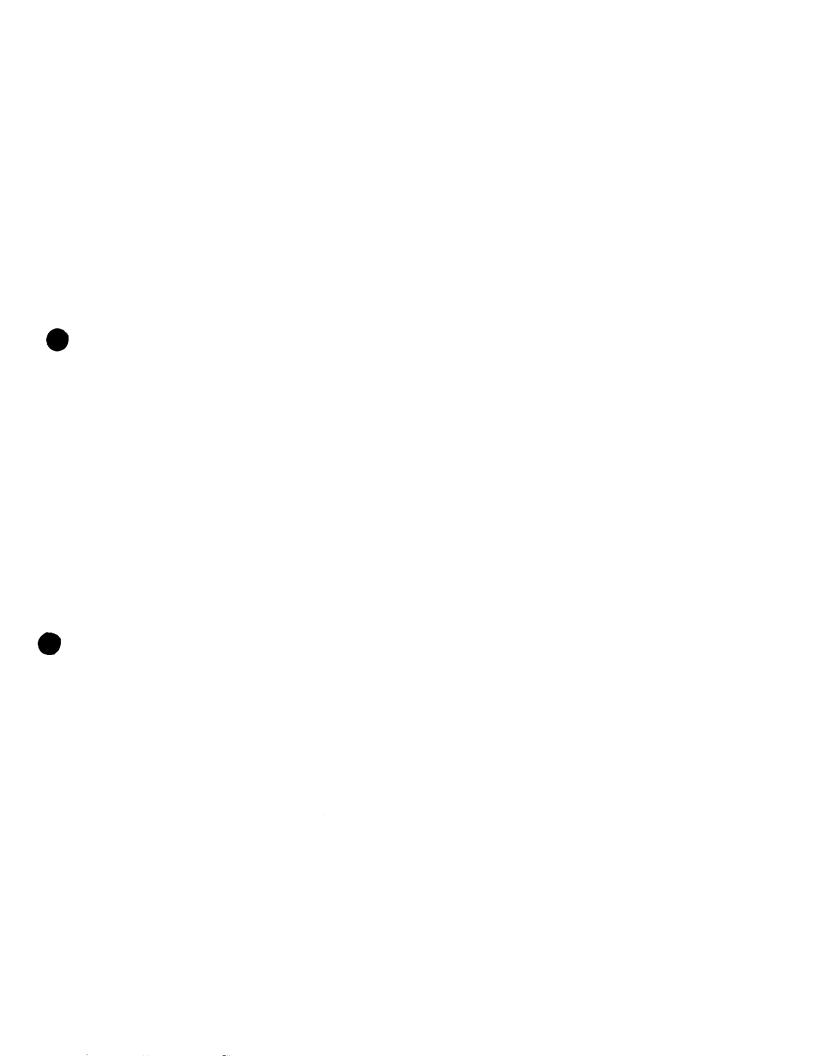
1/1/2003 Appendix 3B Page 5

<sup>+</sup> See chapter 19 for defined terms.

Entiti	ies that have ticked box 34(b)		
38	Number of securities for which functation is sought		
39	Class of *securities for which quotation is sought		
40	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?  If the additional securities do not rank equally, please state:  • the date from which they do  • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment		
41	Reason for request for quotation now  Example: In the case of restricted securities, end of restriction period  (if issued upon conversion of another security, clearly identify that other security)		
42	Number and *class of all *securities quoted on ASX (including the securities in clause 38)	Number	+Class

Appendix 3B Page 6 1/1/2003

<sup>+</sup> See chapter 19 for defined terms.



#### Quotation agreement

- <sup>†</sup>Quotation of our additional <sup>†</sup>securities is in ASX's absolute discretion. ASX may quote the <sup>†</sup>securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

1/1/2003 Appendix 3B Page 7

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before †quotation of the †securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here:

Natalie Korchev

Date: 8 October 2003

Company secretary

Print name:

Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.

14 October 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

#### Appendix 3Y - Change of Director's Interest Notices

Please find enclosed Change of Director's Interest Notices for Mark Diamond and Robert W Moses.

Yours sincerely

Natalie Korchev Company Secretary

Rule 3.19A.2

# Appendix 3Y

## **Change of Director's Interest Notice**

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 30/9/2001.

Name of entity:	Antisense Therapeutics Limited	d	
ABN:	41 095 060 745		

We (the entity) give ASX the following information under listing rule 3.19A.2 and as agent for the director for the purposes of section 205G of the Corporations Act.

Name of Director	Mark Diamond	
Date of last notice	11 December 2002	

#### Part 1 - Change of director's relevant interests in securities

In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Note: In the case of a company, interests which come within paragraph (i) of the definition of "notifiable interest of a director" should be disclosed in this part.

Direct or indirect interest	Direct	
Nature of indirect interest (including registered holder) Note: Provide details of the circumstances giving rise to the relevant interest.	Mark Diamond is the managing director of Antisense Therapeutics Limited	
Date of change	8 October 2003	
No. of securities held prior to change	176,666 ordinary shares fully paid 75,000 options expiring 1/2/07 exercisable at 20 cents each 3,000,000 restricted options expiring 31/7/05 exercisable at 20 cents each	
Class	Fully paid ordinary shares	
Number acquired	23,077	
Number disposed	-	
Value/Consideration  Note: If consideration is non-cash, provide details and estimated valuation	\$3,000 (i.e. 13 cents per share)	

<sup>+</sup> See chapter 19 for defined terms.

11/3/2002

Appendix 3Y Page 1

No. of securities held after change	199,743 ordinary shares fully paid 75,000 options expiring 1/2/07 exercisable at 20 cents each
	3,000,000 restricted options expiring 31/7/05 exercisable at 20 cents each
Nature of change Example: on-market trade, off-market trade, exercise of options, issue of securities under dividend reinvestment plan, participation in buy-back	Acquisition of ordinary shares under the company's share purchase plan.

#### Part 2 – Change of director's interests in contracts

Note: In the case of a company, interests which come within paragraph (ii) of the definition of "notifiable interest of a director" should be disclosed in this part.

Detail of contract	N/A
Nature of interest	N/A
Name of registered holder (if issued securities)	N/A
Date of change	N/A
No. and class of securities to which interest related prior to change Note: Details are only required for a contract in relation to which the interest has changed	N/A
Interest acquired	N/A
Interest disposed	N/A
Value/Consideration Note: If consideration is non-cash, provide details and an estimated valuation	N/A
Interest after change	N/A

Appendix 3Y Page 2 11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

Rule 3.19A.2

# Appendix 3Y

## **Change of Director's Interest Notice**

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 30/9/2001.

Name of entity:	Antisense Therapeutics Limited
ABN:	41 095 060 745

We (the entity) give ASX the following information under listing rule 3.19A.2 and as agent for the director for the purposes of section 205G of the Corporations Act.

Name of Director	Robert W Moses
Date of last notice	15 January 2002

#### Part 1 - Change of director's relevant interests in securities

In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Note: In the case of a company, interests which come within paragraph (i) of the definition of "notifiable interest of a director" should be disclosed in this part.

Direct or indirect interest	Direct (jointly with Lorraine Sandra Moses)	
Nature of indirect interest (including registered holder) Note: Provide details of the circumstances giving rise to the relevant interest.	Robert Moses is the non-executive chairman of Antisense Therapeutics Limited	
Date of change	8 October 2003	
No. of securities held prior to change	250,000 ordinary shares fully paid 125,000 options expiring 1/2/07 exercisable at 20 cents each 250,000 restricted options expiring 31/7/05 exercisable at 20 cents each	
Class	Fully paid ordinary shares	
Number acquired	38,462	
Number disposed	-	
Value/Consideration Note: If consideration is non-cash, provide details and estimated valuation	\$5,000 (i.e. 13 cents per share)	

<sup>+</sup> See chapter 19 for defined terms.

11/3/2002 Appendix 3Y Page 1

No. of securities held after change	288,462 ordinary shares fully paid 125,000 options expiring 1/2/07 exercisable at 20 cents each	
	250,000 restricted options expiring 31/7/05 exercisable at 20 cents each	
Nature of change Example: on-market trade, off-market trade, exercise of options, issue of securities under dividend reinvestment plan, participation in buy-back	Acquisition of ordinary shares under th company's share purchase plan.	e

### Part 2 - Change of director's interests in contracts

Note: In the case of a company, interests which come within paragraph (ii) of the definition of "notifiable interest of a director" should be disclosed in this part.

Detail of contract	N/A
Nature of interest	N/A
Name of registered holder (if issued securities)	N/A
Date of change	N/A
No. and class of securities to which interest related prior to change  Note: Details are only required for a contract in relation to which the interest has changed	N/A
Interest acquired	N/A
Interest disposed	N/A
Value/Consideration  Note: If consideration is non-cash, provide details and an estimated valuation	N/A
Interest after change	N/A

Appendix 3Y Page 2 11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

2004 NOV 16 P 12: 19

OFFICE OF INTERMATION CORPORATE SUPPLY

Rule 4.7B

# **Appendix 4C**

## Quarterly report for entities admitted on the basis of commitments

Introduced 31/3/2000. Amended 30/9/2001

Name of	enti	ŀУ
---------	------	----

ANTISENSE THERAPEUTICS LIMITED

ABN

41 095 060 745

Quarter ended ("current quarter")

30 SEPTEMBER 2003

#### Consolidated statement of cash flows

			Current quarter	Year to date
Cash flows related to operating activities			(3 months)	
			\$A'000	\$A'000
1.1	Receipts from c	ustomers	461	461
1.2	Payments for	(a) staff costs	(370)	(370)
		(b) advertising and marketing (c) research and development	(699)	(699)
		(d) leased assets	-	-
		(e) other working capital	(183)	(183)
1.3	Dividends recei	ived	-	-
1.4	Interest and o	ther items of a similar nature	103	103
1.5	Interest and oth	er costs of finance paid	•	-
<ul><li>1.6 Income taxes paid</li><li>1.7 Other (provide details if material)</li></ul>		-	-	
		,		
	- R & D Tax re	fund received from ATO	375	375
	Net operating	cash flows	(313)	(313)

<sup>+</sup> See chapter 19 for defined terms.

		Current quarter \$A'000	Year to date (three months) \$A'000
1.8	Net operating cash flows (carried forward)	(313)	(313)
	Cash flows related to investing activities		
1.9	Payment for acquisition of:		-
	(a) businesses (item 5) (b) equity investments	-	-
	(c) intellectual property		-
	(d) physical non-current assets		-
	(e) other non-current assets	-	-
1.10	Proceeds from disposal of:		
	(a) businesses (item 5)	-	•
	(b) equity investments	-	-
	(c) intellectual	-	-
	property	-	-
	(d) physical non- current assets		-
	(e) other non-current assets	-	-
1.11	Loans to other entities	-	-
1.12	Loans repaid by other entities	-	-
1.13	Other (provide details if material)	·	
	Net investing cash flows	-	-
1.14	Total operating and investing cash flows	(313)	(313)
	Cash flows related to financing activities		
1.15	Proceeds from issues of shares, options, etc.	4,001	4,001
1.16	Proceeds from sale of forfeited shares	-	•
1.17	Proceeds from borrowings	-	-
1.18	Repayment of borrowings	-	-
1.19	Dividends paid	(100)	(100)
1.20	Other - costs relating to issue of shares	(188)	(188)
	Net financing cash flows	3,813	3,813
	Net increase (decrease) in cash held	3,499	3,499
1.21	Cash at beginning of quarter/year to date	6,546	6,546
1.22	Exchange rate adjustments to item 1.20	-,	•
		10,045	

Appendix 4C Page 2 30/9/2001

<sup>+</sup> See chapter 19 for defined terms.

# Payments to directors of the entity and associates of the directors Payments to related entities of the entity and associates of the related entities

		Current quarter \$A'000
1.24	Aggregate amount of payments to the parties included in item 1.2	463
1.25	Aggregate amount of loans to the parties included in item 1.11	-

1.26	Evolunation	necessary for an	understanding	of the	transactions
1.20	Explanation	necessary for an	i understanding	or me	transactions

Item 1.24 Reflects the following related party payments:

- (a) Total amounts paid to directors include director's fees, salaries and superannuation of \$125,217 (YTD: \$125,217).
- (b) Dr Stanley Crooke, a director of the Company is also a director of Isis Pharmaceuticals Inc ("Isis"). A total amount of \$108,994 (YTD: \$108,994) was paid to Isis for research and development related services provided by them to Antisense Therapeutics Limited ("ATL").
- (c) Professor George Werther, a director of the company, is an executive officer of the Murdoch Childrens Research Institute ("MCRI"). An amount of \$229,070 (YTD: \$229,070) was paid to the MCRI for research services performed by them for ATL.

#### Non-cash financing and investing activities

2.1	Details of financing and investing transactions which have had a material effect on consolidated
	assets and liabilities but did not involve cash flows

assets and habitities but did not involve cash flows
Not applicable.

2.2	Details of outlays made by other entities to establish or increase their share in businesses in which
	the reporting entity has an interest

, , , , , , , , , , , , , , , , , , , ,	 	
Not applicable.		

#### Financing facilities available

Add notes as necessary for an understanding of the position. (See AASB 1026 paragraph 12.2).

		Amount available \$A'000	Amount used \$A'000
3.1	Loan facilities	-	-
3.2	Credit standby arrangements	-	-

<sup>+</sup> See chapter 19 for defined terms.

30/9/2001 Appendix 4C Page 3

#### Reconciliation of cash

show	nciliation of cash at the end of the quarter (as in in the consolidated statement of cash flows) to elated items in the accounts is as follows.	Current quarter \$A'000	Previous quarter \$A'000
4.1	Cash on hand and at bank	1,545	1,546
4.2	Deposits at call	8,500	5,000
4.3	Bank overdraft	-	•
4.4	Other (provide details)	-	-
	Total: cash at end of quarter (item 1.23)	10,045	6,546

#### Acquisitions and disposals of business entities

		Acquisitions (Item 1.9(a))	Disposals (Item 1.10(a))	
5.1	Name of entity	Not applicable	Not applicable	
5.2	Place of incorporation or registration			
5.3	Consideration for acquisition or disposal			
5.4	Total net assets			
5.5	Nature of business			

#### Compliance statement

- 1 This statement has been prepared under accounting policies which comply with accounting standards as defined in the Corporations Act (except to the extent that information is not required because of note 2) or other standards acceptable to ASX.
- 2 This statement does give a true and fair view of the matters disclosed.

Sign here:

Natalie Korchev.....

Date: 20 October 2003

Print name:

Natalie Korchev

Company secretary

Appendix 4C Page 4 30/9/2001

<sup>+</sup> See chapter 19 for defined terms.

#### **Notes**

- 1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity wanting to disclose additional information is encouraged to do so, in a note or notes attached to this report.
- 2. The definitions in, and provisions of, AASB 1026: Statement of Cash Flows apply to this report except for the paragraphs of the Standard set out below.
  - 6.2 reconciliation of cash flows arising from operating activities to operating profit or loss
  - 9.2 itemised disclosure relating to acquisitions
  - 9.4 itemised disclosure relating to disposals
  - 12.1(a) policy for classification of cash items
  - 12.3 disclosure of restrictions on use of cash
  - 13.1 comparative information
- 3. Accounting Standards. ASX will accept, for example, the use of International Accounting Standards for foreign entities. If the standards used do not address a topic, the Australian standard on that topic (if any) must be complied with.

30/9/2001 Appendix 4C Page 5

<sup>+</sup> See chapter 19 for defined terms.



20 October 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Cash Reserves of \$15.4 million, no borrowings

Earlier today Antisense Therapeutics Limited (ASX: ANP) released its September 2003 quarterly cash flow report (Appendix 4C) disclosing that the company's cash balance as at the end of that quarter was \$10 million. We wish to inform the market that due to the allotment of shares on 8 October 2003 (pursuant to the company's share purchase plan) raising \$5.4 million, Antisense Therapeutics cash reserves are currently \$15.4 million. This cash balance excludes the \$1 million subscribed for by Circadian Technologies Limited in the company's August 2003 private placement, which is subject to shareholder approval at Antisense Therapeutics' Annual General Meeting on 31 October 2003.

As previously announced, the funds raised through the private placement and the share purchase plan will be applied to further progress Antisense Therapeutics' drug development projects: ATL1102 for multiple sclerosis, ATL1101 for psoriasis and other drug discovery activities.

Yours sincerely

Natalie Korchev Company Secretary

#### About Antisense Therapeutics Limited

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), which is in Phase I human clinical trials, and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Further company details are available on the Antisense Therapeutics website.

Contact Information: Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999





31 October 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

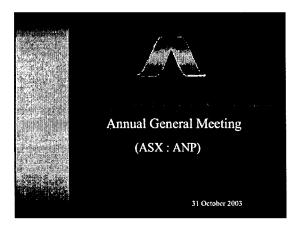
Dear Sir/Madam

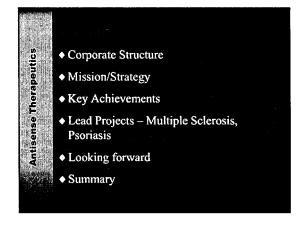
Re: Annual General Meeting 2003 - Presentation

Please find enclosed the presentation to be made to shareholders this morning at Antisense Therapeutics Limited's Annual General Meeting.

Yours sincerely

Natalie Korchev Company Secretary





Listed on ASX Dec 2001
Total funds raised to date: \$28.5 M
Market Capitalisation: \$43.4 M (undiluted)
Key Sharcholders
- Circadian 20%
- Syngene 15% (42% Circadian)
- Isis 11%
- QIC 5%
Cash reserves of \$15.4 M, no borrowings

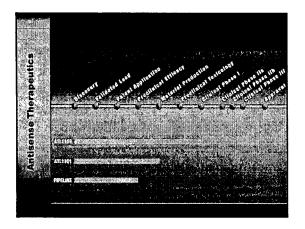
Create, develop and commercialize novel antisense pharmaceuticals for large unmet markets.

Soprades technology of the control o

- ♦ Leverage 13 years of Isis antisense technology development
- ◆ Fast track existing lead projects through pre-clinical and clinical development
- Create pipeline of new antisense therapeutics
- ◆ Commercialise those that are successful in clinical testing via licensing/partnering

Antisense Therapeutics

- ◆ ATL1102 commenced Phase I safety study in humans
- ◆ ATL1101 completed preclinical efficacy program
- ◆ Awarded A\$1.1M Start Grant
- ◆ Capital Raising A\$15M
- Pipeline Undertaken multiple animal studies on antisense compounds for new indications



Antisense Therapeutics

- Disease & Market
  - Life-long chronic disease of the central nervous system
  - Global drug sales of > US\$2.5bn in 2002
  - Need for more effective drug with less side effects
- ◆ Product
  - Antisense inhibitor to VLA-4 protein which contributes to onset of disease
  - Biogen monoclonal ab to VLA-4 in Phase III
  - Anticipate efficacy, dosing and cost advantages

Antisense Therapeutics

#### Progress

- Confirmed activity in pre-clinical murine models of MS
- Confirmed activity also in arthritis and asthma models
- Completed package of pre-clinical animal studies (incl. toxicology)
- Manufactured drug product for Phase I and IIa studies
- Commenced Phase I human trial



#### Outlook

Following successful completion of Phase I trial, Phase IIa trials in 2004

Antisense Therapeutics

#### • Disease & Market

- Chronic non-contagious skin disorder
- Affects 1-2% of population
- Global drug sales forecaset to exceed USS2 billion by 2007 (Frost & Sullivan)
- Need for more effective therapies

#### • Product

- Antisense inhibitor to IGF-1R regulates cell growth
- Developing topical formulation

Antisense Therapeutics

#### ◆ Progress

- Selected antisense lead inhibitor
- Prepared topical formulation
- Confirmed cream active in psoriasis skin grafts
- Completed pre-clinical efficacy program
- Awarded A\$1.1 million government grant

#### Outlook

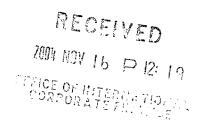
- Commence "Proof of Concept" study in psoriasis patients in 2004

Project	Value Driver	Timing
ATL1102 (MS)	◆Complete Phase 1 ◆ Start Phase IIa ◆ Partnering objective	1 <sup>st</sup> half '04 2 <sup>nd</sup> half '04 Concl Ph IIa
ATL1101 (Psoriasis)	◆Complete product manufacture and toxicology program ◆Start "Proof of Concept" study ◆Partnering objective	1st half '04 2nd half '04 Concl "PoC"
Pipeline Research	Complete multiple animal studies with new antisense leads     Objective: to partner a compound at pre-clinical stage	Ongoing  By end 2005

Antisense Therapeutics

- ◆ Significant progress in R&D activities
- ♦ Strong cash position allowing ANP to reach key milestones on lead projects
- ♦ Effective leveraging of partnerships to expedite R&D programs and reduce development cost and risk
- ♦ Clear commercialisation objectives

High growth potential/reduced technical risk



31 October 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

#### Results of Annual General Meeting: 31 October 2003

In accordance with Listing Rule 3.13.2, Antisense Therapeutics Limited advises that the resolutions as set out in its Notice of General Meeting, which was lodged with the ASX on 26 September 2003, were put to that meeting today and were carried on a show of hands.

Validly appointed proxies totalling 157,835,597 shares, representing 45.41% of the total issued shares in the Company, were received. The proxies were to be exercised as follows:

	In Favour	Against	Abstention	Others' <u>Discretion</u>	Chairman's <u>Discretion</u>			
Ordinary Resolution 1 - Re-elect as director Dr Chris Belyea								
Percentage of proxies	99.32%	-	-	0.03%	0.65%			
No. of shares represented by proxies	156,754,558	-	-	48,462	1,032,577			
Ordinary Resolution 2 - Re-elect as dir	ector Prof Geor	ge Werthei	r					
Percentage of proxies	99.32%	-	-	0.03%	0.65%			
No. of shares represented by proxies	156,754,558	-	-	48,462	1,032,577			
Ordinary Resolution 3 - Approval of Issue of Shares to Polychip Pharmaceuticals Pty Ltd								
Percentage of proxies	58.27%	0.07%	41.45%	0.04%	0.18%			
No. of shares represented by proxies	91,964,281	106,262	65,427,776	58,462	278,816			

	In Favour	<u>Against</u>	Abstention	Others' <u>Discretion</u>	Chairman's <u>Discretion</u>	
Ordinary Resolution 4 - Ratification of Prior Issue of Shares						
Percentage of proxies	82.76%	0.02%	17.01%	0.04%	0.18%	
No. of shares represented by proxies	130,621,911	29,185	26,847,223	58,462	278,816	

Yours faithfully

Natalie Korchev Company Secretary RECEIVED

2004 NOV 16 P 12: 20

5 November 2003

OFFICE OF IMTERNATIONS CORPORATE FINATURE

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

CIRCADIAN
TECHNOLOGIES
LIMITED
ABN 32 006 340 567

10 Wallace Avenue, Toorak Victoria 3142 Australia

P.O. Box 23, Toorak, Victoria 3142 Australia

Telephone: +61 3 9826 0399 Fax: +61 3 9824 0083

No of Pages: 4

Dear Sir/Madam

Re: Change in Substantial Holding for Antisense Therapeutics Limited

We enclose Form 604 "Notice of Change of Interests of Substantial Holder" with respect to an investment in Antisense Therapeutics Limited by Polychip Pharmaceuticals Pty Ltd (a wholly owned subsidiary of Circadian Technologies Limited).

Yours sincerely

Natalie Korchev

Company Secretary

N. Korcher

#### FORM 604 Corporations Act 2001 Section 671B

#### NOTICE OF CHANGE OF INTERESTS OF SUBSTANTIAL HOLDER

To:

ANTISENSE THERAPEUTICS LIMITED ('ATL')

ACN:

095 060 745

#### 1. Details of substantial holder (1)

Name:

POLYCHIP PHARMACEUTICALS PTY LTD (A WHOLLY OWNED

SUBSIDIARY OF CIRCADIAN TECHNOLOGIES LIMITED)

ACN:

006 455 456

There was a change in the interests

of the substantial holder on

31/10/2003

The previous notice was

given to the company on

11/12/2002

The previous notice was dated

11/12/2002

#### 2. Previous and present voting power

The total number of votes attached to all the voting shares in the company or voting interests in the scheme that the substantial holder or an associate (2) had a relevant interest (3) in when last required, and when now required, to give a substantial holding notice to the company or scheme, are as follows:

Class of securities (4) Previous notice * Pre		ties (4) Previous notice *		ent notice	
	Person's votes	Voting power (5)	Person's votes	Voting power (5)	
Ordinary	64,708,338	23.51%	72,436,800	20.39% (voting power reduced as a result of share placements by ATL of a total of 72,279,842 shares in August and October 2003).	

#### 3. Changes in relevant interests

Particulars of each change in, or change in the nature of, a relevant interest of the substantial holder or an associate in voting securities of the company or scheme, since the substantial holder was last required to give a substantial holding notice to the company or scheme are as follows:

Date of change	Person whose relevant interest changed	Nature of change (6)	Consideration given in relation to change (7)	Class and number of securities affected	Person's votes affected (no. of shares)
8/10/03	Polychip Pharmaceuticals P/L	Share Purchase Plan	\$0.13	Ordinary shares	38,462
31/10/03	Polychip Pharmaceuticals P/L	Share Placement	\$0.13	Ordinary shares	7,690,000

#### 4. Present relevant interests

Particulars of each relevant interest of the substantial holder in voting securities after the change are as follows:

Holder of relevant interest	Registered holder of securities	Person entitled to be registered as holder (8)	Nature of relevant interest (6)	Class and number of securities	Person's votes
Polychip Pharmaceuticals Pty Ltd	Polychip Pharmaceuticals Pty Ltd	Polychip Pharmaceuticals Pty Ltd	Beneficial Owner	Ordinary shares 72,436,800	72,436,800

#### 5. Changes in association

The persons who have become associates (2) of, ceased to be associates of, or have changed the nature of their association (9) with, the substantial holder in relation to voting interests in the company or scheme are as follows:

Name and ACN (if applicable)	Nature of association
Not applicable	

## 6. Addresses

The addresses of persons named in this form are as follows:

Name	Address (Registered Office)
Polychip Pharmaceuticals Pty Ltd	Rialto Towers, Level 23, 525 Collins Street, Melbourne
Circadian Technologies Limited	Rialto Towers, Level 23, 525 Collins Street, Melbourne

Signature		
Print Name	: Natalie Korchev	Capacity: Company Secretary
Sign here	N. Korchav	Date 5/11/2003

7 November 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Appendix 3B: Issue of shares approved at 2003 AGM

On 20 August 2003, Antisense Therapeutics Limited announced the completion of a placement of shares to Australian institutions and other professional investors, raising \$5 million. This placement included a subscription by Polychip Pharmaceuticals Pty Ltd (a wholly owned subsidiary of Circadian Technologies Limited) ("Polychip") for 7,690,000 fully paid ordinary shares for a total consideration of \$999,700, which was subject to shareholder approval.

On 31 October 2003, at the company's AGM, shareholders approved this issue of shares to Polychip and these shares were allotted on 6 November 2003. Accordingly, an Appendix 3B "New Issue Announcement, Application for Quotation of Additional Securities" follows.

Yours sincerely

Natalie Korchev Company Secretary

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

# Appendix 3B

# New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002, 1/1/2003.

Name of entity

Antisense Therapeutics Limited			
ABN	95 060 745		
	73 000 743		
We (the entity) give ASX the following information.			
Part 1 - All issues You must complete the relevant sections (attach sheets if there is not enough space).			
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	Ordinary Shares (ANP)	
2	Number of <sup>+</sup> securities issued or to be issued (if known) or maximum number which may be issued	7,690,000	
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	Fully paid ordinary shares.	

1/1/2003 Appendix 3B Page 1

<sup>+</sup> See chapter 19 for defined terms.

4 Do the \*securities rank equally in all respects from the date of allotment with an existing \*class of quoted \*securities?

If the additional securities do not rank equally, please state:

- the date from which they do
- the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment
- the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment

Yes N/A

5 Issue price or consideration

7,690,000 shares at \$0.13 per ordinary share amounting to a total consideration of \$999,700.

6 Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets) Share placement to Polychip Pharmaceuticals Pty Ltd (who participated in the company's August 2003 private share placement to institutions and other professional investors), issuing 7,690,000 shares at \$0.13 per share. The funds raised through the placement will be applied to the company's drug development projects: ATL1102 for multiple sclerosis, ATL1101 for psoriasis and other drug discovery activities.

The issue of these shares to Polychip Pharmaceuticals (a wholly owned subsidiary of Circadian Technologies Limited) was approved by shareholders at the company's AGM on 31 October 2003.

Dates of entering \*securities into uncertificated holdings or despatch of certificates 6 November 2003

8 Number and \*class of all \*securities quoted on ASX (including the securities in clause 2 if applicable)

Number	+Class
221,940,842	Ordinary Shares (ANP)
91,467,765	Options (ANPO)

Appendix 3B Page 2

<sup>+</sup> See chapter 19 for defined terms.

Appendix 3B Page 3

Number +Class 133,312,508 Number and +class of all Restricted ordinary shares (ANPAK) +securities not quoted on ASX Restricted options expiring 31 (including the securities in clause 11,500,000 2 if applicable) July 2005 exercisable at 20 cents (ANPAM) 20,000,000 Restricted options expiring 30 November 2006 exercisable at 20 cents (ANPAO) 2,450,000 Options expiring 31 July 2005 exercisable at 20 cents (ANPAQ) 10 Dividend policy (in the case of a N/A trust, distribution policy) on the increased capital (interests) Part 2 - Bonus issue or pro rata issue Is security holder approval N/A required? 12 Is the issue renounceable or non-N/A renounceable? 13 Ratio in which the \*securities will be offered +Class of +securities to which the N/A 14 offer relates \*Record N/A 15 date to determine entitlements 16 Will holdings on different registers N/A (or subregisters) be aggregated for calculating entitlements? Policy for deciding entitlements in N/A 17 relation to fractions 18 Names of countries in which the N/A entity has \*security holders who will not be sent new issue documents Note: Security holders must be told how their entitlements are to be dealt with. Cross reference: rule 7.7. 19 Closing date for receipt N/A acceptances or renunciations

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a broker and accept for the balance?	N/A

Appendix 3B Page 4 1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

		<del></del>
32	How do *security holders dispose of their entitlements (except by sale through a broker)?	N/A
33	<sup>+</sup> Despatch date	N/A
Dar	t 3 - Quotation of secur	rities
	ed only complete this section if you are app	
34	Type of securities (tick one)	
(a)	Securities described in Part 1	
(b)		of the escrowed period, partly paid securities that become fully paid, employee ends, securities issued on expiry or conversion of convertible securities
Enti	ties that have ticked box 34(a	a)
Addi	tional securities forming a new cla	ass of securities
Tick to	o indicate you are providing the informa ents	tion or
35		securities, the names of the 20 largest holders of the number and percentage of additional *securities held by
36		by securities, a distribution schedule of the additional or aber of holders in the categories
	1,001 - 5,000 5,001 - 10,000	
	10,001 - 100,000 100,001 and over	
37	A copy of any trust deed for t	he additional *securities

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

Entit	tes that have ticked box 34(b)	)	
38	Number of securities for which quotation is sought		
39	Class of *securities for which quotation is sought		
40	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?		
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment		
41	Reason for request for quotation now  Example: In the case of restricted securities, end of restriction period		
	(if issued upon conversion of another security, clearly identify that other security)		
42	Number and <sup>+</sup> class of all <sup>+</sup> securities quoted on ASX ( <i>including</i> the securities in clause 38)	Number	+Class
	•		

Appendix 3B Page 6

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

### Quotation agreement

- <sup>†</sup>Quotation of our additional \*securities is in ASX's absolute discretion. ASX may quote the \*securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

1/1/2003 Appendix 3B Page 7

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before 'quotation of the 'securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here:

Natalie Korchev

Date: 7 November 2003

Company secretary

Print name:

Natalie Korchev

Appendix 3B Page 8 1/1/2003

<sup>+</sup> See chapter 19 for defined terms.



RECEIVED

MON NOV 16 P 12: 20

OFFICE OF INTERNATIONAL CORPORATE FINANCE

5 December 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

### Re: Securities to be released from escrow

We wish to advise of the forthcoming release from escrow of 133,312,508 ordinary fully paid shares in Antisense Therapeutics Limited and 31,500,000 options over ordinary shares ("options") in the company on 19 December 2003. The ordinary shares to be released from escrow are owned by the company's three largest shareholders: Circadian Technologies Limited (51,656,254 shares), Syngene Limited, (42% owned by Circadian) (51,656,254 shares) and Isis Pharmaceuticals, Inc (the company's technology partner) (30,000,000 shares).

Since the company's listing, its three largest shareholders have been strong supporters of the company with participation in subsequent capital raisings by Antisense Therapeutics. Circadian has subscribed for and been allotted shares for an amount of \$1,774,700 and Isis Pharmaceuticals Inc has been allotted shares for an amount of \$775,000 since the initial public offering.

The options to be released from escrow are owned by Isis Pharmaceuticals (20,000,000 options expiring on 30 November 2006)) and directors and an executive of the company (11,500,000 options expiring on 31 July 2005). Each of these options has an exercise price of 20 cents and they will remain unquoted options.

Yours sincerely

Natalie Korchev Company Secretary



RECEIVED

2004 NOV 16 P 12: 20

CORPORATE THE AND MAL

9 December 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

### **Investor Update**

Antisense Therapeutics Limited (ASX: ANP) is pleased to advise of several positive steps in the development of its drug pipeline.

### In summary:

- Dosing is completed in both single and multiple dose Phase 1 human clinical trials on ATL1102, our second generation antisense drug for multiple sclerosis. We plan to present preliminary data at a neuroscience conference in January 2004
- Preparations are on track for commencement of a "proof of concept" human clinical trial on ATL1101, a second generation antisense cream for psoriasis, in the second half of 2004
- Candidate antisense drugs to treat a range of diseases (details not yet disclosed) are under early-stage evaluation in animal disease models and news on these additional projects will be provided in the near future.

### ATL1102 for multiple sclerosis

ATL1102 is designed to block the synthesis of an immune system component or protein called VLA-4 that is known to play a part in both the onset and progression of multiple sclerosis ("MS").

Phase I human clinical trials of ATL1102 are being conducted at the Charterhouse Clinical Research Unit in London.

The aim of these Phase 1 trials is to obtain information on the pharmacokinetic<sup>1</sup> behaviour of ATL1102 in humans and to assess the safety and tolerability of increasing dose levels of ATL1102 injected as single and multiple doses.

<sup>&</sup>lt;sup>1</sup> "Pharmacokinetics" is how the drug distributes in the body over time after administration, helpful in deciding dosing frequency in future studies

Fifty-four healthy volunteers are participating in the placebo-controlled, randomised, double-blind study.

In August, the company announced that single escalating dosage had commenced. The study has subsequently progressed rapidly, with both single and multiple dosing schedules already complete.

Laboratory investigations of the biological samples collected during the trial are currently taking place. Preliminary data should be available for presentation at the Australian Neuroscience Society Scientific Conference in Melbourne on 30 January 2004. Final results are on schedule to be completed and reported in mid 2004.

Following successful completion of the trial, an application will be made in 2004 to conduct a Phase IIa clinical trial to assess preliminary efficacy of ATL1102 in patients with multiple sclerosis.

MS is a life-long chronic, incurable disease that progressively destroys the central nervous system. It is commonly diagnosed between the ages of 20 and 40 years.

MS affects about 350,000 people in the US alone, where the estimated annual cost of the disease is more than US\$2.5 billion.

ATL1102 may have efficacy, dosing route and cost of therapy advantages over current treatments for MS. ATL1102 and the broad concept of blocking this receptor using antisense was conceived by scientists at Isis Pharmaceuticals, Inc (USA), our key technology partner, and licensed to Antisense Therapeutics on formation of the company in 2001.

### Market Update - ATL1101 for psoriasis

ATL1101 is designed to block the synthesis of the IGF-1 receptor, a protein involved in the regulation of cell growth in psoriasis.

In July 2003, Antisense Therapeutics announced its plans to undertake a "proof of concept" study, which is an accelerated path to testing the activity of ATL1101 in humans suffering from psoriasis.

In this "proof of concept" study, also referred to as the small plaque assay (SPA), a relatively small quantity of ATL1101 will be applied to areas of psoriatic skin on a limited number of patients. The SPA study is supported by an AusIndustry START grant of A\$1.1 million.

The human study can commence once supplies of drug product are manufactured and a limited animal toxicology program is performed.

The manufacture of the active pharmaceutical ingredient and the analytical work required for product release is proceeding well and is likely to be completed by the end of this month. The formulation of injectable and cream presentations of ATL1101 is expected to start in Q1 2004, with toxicology studies scheduled to commence once this is completed.

Subject to receiving the relevant approvals to conduct this trial, the company expects the "proof of concept" study in psoriasis patients to commence in the second half of 2004.

Psoriasis is a chronic, non-contagious skin disorder, which affects 2% of the population.

The worldwide market for psoriasis treatments was more than US\$500 million in 2000 and is forecast to exceed US\$2 billion by 2007 (Frost & Sullivan). There is an acknowledged need for more effective and safer treatments than those currently available.

The concept of blocking the IGF-1 receptor to treat psoriasis was conceived by researchers at the Murdoch Childrens Research Institute in Melbourne and licensed to Antisense for further collaborative development on our formation in 2001.

### **About Antisense Therapeutics Limited**

Antisense Therapeutics is an ASX-listed biopharmaceutical drug discovery and development company, focused on creating, developing and commercialising unique antisense pharmaceuticals for large unmet markets.

Antisense drugs are synthetic, DNA-like compounds designed for use as medicines and to block disease processes with extraordinary precision. Unlike conventional small-molecule medicines - the discovery of which requires time-consuming and laborious trial-and-error - antisense medicines are rationally designed by directly exploiting the huge body of genetic information now available from the human genome project.

Antisense Therapeutics' two most advanced projects target multiple sclerosis (ATL1102) and psoriasis (ATL1101). The company plans to commercialise its pipeline via partnerships with major biotechnology and pharmaceutical companies.

As at 8 December 2003, Antisense has cash reserves of A\$15.9 million following a recent successful private placement and a capital raising by a Shareholder Purchase Plan. Antisense has no borrowings and is forecast to have sufficient funds for its planned activities into 2005.

Antisense Therapeutics' major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Further company details are available from www.antisense.com.au

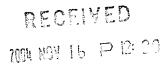
### For further information:

Managing Director Mark Diamond (613) 9827 8999 Company Secretary Natalie Korchev (613) 9827 8999



ASIC

Australian Securities & Investments Commission



### Change to company details

Form 484 — Corporations Act 2001

### **Section C**

Section C may be lodged independently if no changes are to be notified via Sections A or B.

Use this form to notify ASIC of:

C1 Change to share structure table

C2 Issue of shares

C3 Cancellation of shares

C4 Changes to members' register

### **Related Forms**

484 A - change of address, name (officeholders or members), details (ultimate holding company)
484 B - appoint/cease officeholder, change special purpose company status

If there is insufficient space in any section of the form, you may photocopy the relevant page(s) and submit as part of this lodgement

### Company details

### Company name

### ANTISENSE

ACN/ ABN

095

is this document being lodged to update the Annual Company Statement that was sent to you?



### Section C completion guide

### Standard share codes

Refer to the following table for the share class codes for sections C1, C2. C3 and C4

Share cla	ass Full iitle	Share class code	Full title
A	A	PRF	preference
В	Betc	CUMP	cumulative preference
EMP	employee's	NCP	non-cumulative preference
FÓU	founder's	REDP	redeemable preference
LG	life governor's	NRP	non-redeemable preference
MAN	management	CRP	cumulative redeemable preference
ORD	ordinary	NCRP	non-cumulative redeemable preference
RED	redeemable	PARP	participative preference
SPE	special		

Continues on next page...

ASIC Form 484 Section C 1 July 2003

If you are using the standard share class codes you do not need to provide a full title for the shares. If you are not using the standard share class code, enter a code of no more than 4 letters and then show the full title.

Page 1 of 9

### Sections to complete

Use the table below to identify the sections of this form to complete (please indicate the sections that have been completed). Completion of this table is optional.

		C1 - Change to share structure table	C2 - Issue of shares	C3 - Cancellation of shares	C4 - Change to members register
	Issue of shares				
	Proprietary company	y was	1	Not required	
FF T	Public company				
	If in response to the Annual company statement		American Carlo	Not required	<b>√</b> ## to the following the second of the se
	if not in response to the Annual company statement	Not required		Not required	Not required
	Cancellation of shares				
	Proprietary company	1	Not required		1
N. P. S. C.	Public company				
	if in response to the Annual company statement		Not required	<b>V</b>	
	if not in response to the Annual company statement	Not required	Not required		Not required
	Transfer of shares				
$\Box$	Proprietary company	Not required	Not required	Not required	
	- Public company				
	if in response to the Annual company statement	Not required	Not required	Not required	
	if not in response to the Annual company statement	Not required	Not required	Not required	Not required
	Changes to amounts paid				
	Proprietary company	1/	Not required	Not required	
	- Public company				
	if in response to the Annual company statement		Not required	Not required	
	If not in response to the Annual company: statement	Not required	Not required	Not required	Not required
	Changes to beneficial ownership				
	Proprietary company	Not required	Not required	Not required	<b>/</b>
i makalaha Marana	→ Public company				
	if in response to the Annual company statement	Not required	Not required:	Not required	1
	if not in response to the Annual company statement	Not required	Not required	Not required	Not required

To notify ASIC about a division or conversion of a class of shares, you must lodge a form,211.

To notify ASIC about a conversion of shares into larger or smaller numbers; you must lodge a form 2205.

or original original original capital

Where the share class has changed (eg. as a result of the issue or cancellation or shares), please show the updated details for this share class in the table below. Details of share classes that have not changed are not required here.

edin a katherines side	Full title if not standard	Total number issued	Total amount paid on these shares	Total amount unpaid on these shares
ORD	ORDINARY FULLY PAID SHARES OPHONS OVER ORDINARY SHARES	355,253,350	35,105,871-53	0
OPTIONS	OPTIONS OVER ORDINARY SHARES	125,417,665	789,759.95	n
				्र स्थार
		Tage was too all the standard regions.	Mark Control of American Control	## 35 3 april
Earliest date of chance Please indicate the earl	je est date that any of the above changes occured			

### C2 Issue of shares

List details of new share issues in the following table.

Share class code	Number of shares issued	Amount paid per share	Amount unpaid per share	
ORD	41,508,302	\$ 0.13	0	
ORD	1,000	\$0.20	0	
ORD	7,690,000	\$0.13	0	
yeer was a week a sales		AND THE REPORT OF THE PARTY OF		
A SAFATON AND SPACE AND A CHESK C.			自一一部一部的特别的新国际特别的特别的 计对象 化自己基础的 医电影	الى دەرايىيىن ئاسىرىيىن ئى <b>لىس</b>
0 8110	lest date that any of the above changes	Occured		
lease indicate the ear O & /   O D) [M	iest date that any of the above changes 」ルロコ 机 口が み			
ease indicate the ear D S / D D	iest date that any of the above changes 」ルロコ 机 口が み	occured all of the shares issued under a written contrac	<b>17</b>	

(fr.no; proprietary companies are not required to provide any further documents with this form. Public companies must also lodge a Form.

or oancenation of states

Reason for cancellation Please indicate the reason that shares have been cancelled (select one or more boxes)

Detai	ام وا	fcar	الممر	Δd	cha	rac
Detai	13 L	H L.AI	ıcen		SHA	res

≓: Redeemable preference: snares ⇒ S:254J ☐ Redeemed out of profits	
Redeemed out of proceeds of a fresh issue of shares	
Capital reduction—S.256A—S.256E	AND
Single shareholder.company	
:Múltiple shareholder company:A.Form 2560 must be lodged before a capital reduction takes place:	PARTITUDE OF THE STATE OF THE S
Share buy-back:=ss:257H(3);	A STATE OF THE STA
Other buy back type: A form 280 or 281 must be lodged at least 14 days; and	
no more than 1 year before the share buy-back can take place	AND THE STATE OF T
Eorfeiled shares S. 258D	APPENDING AND APPENDING AP
FH. Shares returned to a public company—ss:258E(2) & (3)	ANTONIA CANADA C
Undersection:651C:-724(2);-737:0:738	
Undersection:1325A (courtiorder)  Other	NIEST STEEL
Description	GITTA TO THE TOTAL
Give section reference:	MANUAL MA
	THE STATE OF THE S
List the details of shares cancelled in the following table:	AND THE PROPERTY OF THE PROPER
Share class code:: Number of shares cancelled:::Amount paid (cash or otherwise)::	
	ANTENNAME OF THE STATE OF THE S
SOLUE / TESTAN	INALAMAN PAPA INALAMAN PARAMA INALAMAN PARAMAN INALAMAN PARAM
101101 101101 101101 101101 101101 101101	HANTA HAND CORRESPONDED TO THE COMMENT OF THE COMME
STEAT	THE STATE OF THE S
	THE STATE OF THE S
Earlest date of change	
Please indicate the earliest date that any of the above changes occured:	
PO DI M. MITT YI	

### C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (\$178B).
- If shares are jointly owned, provide names and addresses of all joint owners on a separate sheet, clearly indicating the share class and with whom the shares are jointly owned.

Please complete a separate section	below for each member	See attached Annexure A of 4 pages
The changes apply to Please indicate the name and address of the member whose shareholding has changed	OR Company name  ACN/ ARBN/ ABN  Office, unit, level, or PO Box number	Given names
	Street number and Street name  Suburb/City  Postcode  Country (if not Australi	State/Territory
The changes are  Share class Shares Shares code Increased by decrease (number) (number)	Number now Total \$ paid Total \$ ed by held on these unpaid on the shares on the shares	d (y/n) held (y/n) member (y/n) se
Earliest date of change Please indicate the earliest date that any of the above changes occurred	Date D J D M M Y	
Date of entry of member's name in register (New members only)	Date:	
ASIC Form 484 Section C 1 July 2003		Page 5 of 9

### Signature

This form must be signed by a current officeholder of the company.

	I certify that the information in this form is true and complete  Name	Alberta (Alberta de La Companyo de L
	NATALIE KORCHEV	
	Capacity	
	* Company secretary.	
	Signature N. Korchev	
	Date signed 0 2 7 1 2 7 0 3 D. D. M. M. N. Y.	
Lodging party details		A PER SERVICE
• • •	if annihable) and to the an estadion about this fame about he discussed	
Please notify the registered agent details (	if applicable) and to whom queries about this form should be directed.	
Registered Agent details	ASIC registered agent name:	
If this form is being lodged by an ASIC registered agent, please complete agent		
name and number	ASIC registered agent number	
	and the control of th	<u>Sarigo er 14 il 5 salar o Estadori</u>
Queries about this form	If there is a query regarding this form, ASIC should contact (Choose one of the following	$y_{1,2,1,3,1,3,1}$
You can nominate an officeholder, lodging party or ASIC registered agent	★ Signatory above	erio e esta dan esta e Esta da esta esta esta esta esta esta esta est
party critical regions again.	AS/C registered agent above	
	Name of lodging party	
	ANTISENSE THERAPEUTICS LIMITED	
	Office, unit, level, or PO Box number	
	LEVEL 1	
	Street number and Street name	
	10 WALLACE AVENUE	
•	Suburb/Ciry State/Temtory	
	TOORAK VIC Postcode Country (if not Australia)	
	3142	
	DX Number: DX City/suburb:	
	Telephone Number (03) 9827 8999	
	1 (03) 3041 0373	

M

Mail

Send completed and signed forms to: Australian Securities and Investments Commission, PO Box 4000, Gippsland Mail Centre VIC 3841. For help or more information

Telephone 03 5177 3988

Email inf

Web

info.enquiries@asic.gov.au www.asic.gov.au/easylodge

Top 20 for Company Statement Nov 03.xls

## This is annexure A of 4 pages referred Win form 484 Part C "Change to Company stails"

### ANTISENSE THERAPEUTICS LIMITED TOP 20 SHAREHOLDERS AS AT 13 NOVEMBER 2003

	Member's full name & address OR executor's/trustee's full name & address	Share Class Code	Shares Increased by	Shares Num decreased by held	Shares Number now ised by held	Fully Paid (y/n)	Beneficially held (y/n)	Date of Entry of members name in register (New members only)
1	Polychip Pharmaceuticals Pty Ltd ACN 006 455 456 Level 1 10 Wallace Avenue TOORAK VIC 3142	ORD	7,728,462	,	72,436,800	>	>	
7	Syngene Limited ACN 006 161 753 Level 1 10 Wallace Avenue TOORAK VIC 3142	ORD	38,467	•	54,413,467	>	>	
m	Isis Pharmaceuticals Inc ACN - N/A 2292 Faraday Avenue, Carlsbad, CA, 92008 USA (US Listed Company)	ORD		•	40,333,333	<b>&gt;</b>	>	
4	Queensland Investment Corporation ACN: N/A C/- National Nominees Limited, GPO Box 2242, Brisbane, QLD, 4001	ORD	1,845,000	•	15,845,000	>	>	
3	National Nominees Limited ACN 004 278 899 GPO Box 1406M, Melbourne, VIC. 3001	ORD	6,948,422		12,410,000	>	z	
ဖ	Murdoch Childrens Research Institute ACN 006 566 972 10th Floor, Royal Children's Hospital, Flemington Road, Parkville, VIC, 3052	ORD	•	•	10,300,000	>	>	
^	Commonwealth Custodial Services Limited ACN 000 485 487 GPO Box 4122, Sydney, NSW, 1030	ORD	-	000'06	3,243,332	>	z	

# This is annexure A of 4 pages referred n form 484 Part C "Change to Company Details"

## ANTISENSE THERAPEUTICS LIMITED TOP 20 SHAREHOLDERS AS AT 13 NOVEMBER 2003

· ·								Date of Entry of members name in
	Member's full name & address OR executor's/trustee's full name & address	Share Class Code	Shares Increased by	Shares Num decreased by held	Shares Number now ised by held	Fully Paid (y/n)	Beneficially held (y/n)	register (New members only)
80	Spotlight Superannuation Pty Ltd <spotlight a="" c="" fund="" provident=""> ACN 070 073 853 100 Market Street, South Melbourne, VIC. 3205</spotlight>	ORD	38,462	1	2,071,795	>	>	
6	Link Traders (Aust) Pty Ltd ACN 002 065 849 Unit 405, 25 Lime Street, Sydney, NSW. 2000	ORD	•	l	2,000,000	>	>	
10	Mr Joshua Andrew Eagle 108 Park Road, Wooloowin, QLD 4030	ORD	774,286	1	1,974,286	>	>	
11	Mr Guo Liang Li & Mrs Jie Ling Bu PO Box 3742 Marsfield NSW 2122	ORD	1,510,908		1,510,908	>	>	27-Aug-03
12	Bow Lane Nominees Pty Ltd ACN 005 734 145 C/- Smith Barney Citigroup Australia Pty Ltd PO Box 360, Collins Street West, Vic, 8007	ORD	1,250,000		1,500,000	>	Z	
13	Danewell Pty Ltd <danewell a="" business="" c=""> ACN 078 417 651 100 Market Street, South Melbourne, VIC, 3205</danewell>	ORD	•	1	1,276,924	>	>	·
4	Monit Nominees Pty Ltd <fraid a="" c="" family=""> ACN 005 373 615 100 Market Street, South Melbourne, VIC, 3205</fraid>	ORD	38,462		1,205,128	>	>	
15	Berne No. 132 Nominees Pty Ltd <1000355 A/C> ACN 010 413 591 GPO Box 202, Brisbane, QLD, 4001	ORD	,	175,000	1,175,000	>	>	
16	ANZ Nominees Limited ACN 005 357 568 GPO Box 2842AA, Melbourne, VIC 3001	ORD	491,241		1,044,241	>	Z	

## Top 20 for Company Statement Nov 03.xls

## This is annexure A of 4 pages referred (An form 484 Part C "Change to Company Patails"

## ANTISENSE THERAPEUTICS LIMITED TOP 20 SHAREHOLDERS AS AT 13 NOVEMBER 2003

	Member's full name & address OR executor's/trustee's full name & address	Share Class Code	Shares Increased by	Shares Num	Shares Number now ised by held	Fully Paid (y/n)	Beneficially held (y/n)	Date of Entry of members name in register (New
11	All-States Finance Pty Ltd ACN 004 452 153 Suite 2502, Quay West Apts 98 Gloucester Street, Sydney, NSW 2000	ORD	1,038,462	•	1,038,462	<b>&gt;</b>	>	8-Sep-03
18	1	ORD	950,000	•	950,000	>	>	3-Sep-03
19	Mrs Tung Yueh-Ying Tsai 50 Monomeath Avenue, Canterbury, VIC 3126	ORD	000'006	•	900,000	>	>	18-Jul-03
20	Mrs Lisa Steven 7 Kinkora Road, Hawthorn, VIC, 3122	ORD	38,462	•	803,462	>	>	

# This is annexure A of 4 pages referred in form 484 Part C "Change to Company Details"

ANTISENSE THERAPEUTICS LIMITED TOP 20 SHAREHOLDERS AS AT 13 NOVEMBER 2003

Member's full name & address OR executor's/trustee's full sname & address	Share Class Code	Shares Increased by	Shares Num	Shares Number now sed by held	Fully Paid (y/n)	Beneficially held (y/n)	Date of Entry of members name in register (New members only)
MEMBERS NO LONGER ON TOP 20 AS AT 13 NOVEMBER 2003							
DBR Corporation Pty Ltd ACN 082 015 950 Level 2, 33 Park Street, South Melbourne, Vic 3205	ORD	,	196,538	753,462			
Jagen Pty Ltd ACN 005 137 851 Level 9 South, 161 Collins Street, Melbourne, VIC. 3000	ORD	•	•	750,000			
Invia Custodian Pty Limited <jbw 2="" a="" c="" international="" no.="">ACN 006 127 984 C/- M3788015Q IPNM GPO Box 4595 SS, Melbourne, VIC. 3001</jbw>	ORD	-	950,000	0			
BCI Holdings Pty Ltd ACN 078 359 001 3 Woodmason Street, Malvern, VIC 3144	ORD	,	719,666	0			
Bowyang Nominees Pty Ltd ACN 000 932 507 Salomon Smith Barney Australia Securities Pty Ltd GPO Box 557, Sydney, NSW 2001	ORD	,	1,343,635	0			
S H R Pty Ltd ACN 006 609 418 Level 50, Rialto South Tower, 525 Collins Street, Melbourne, VIC 3000	ORD		1,500,000	0			

Signed: Natalie Korchev Company Secretary

2 11212003

Date:

### ANTISENSE THERAPEUTICS

2 December 2003

Sent via Express Post

Australian Securities & Investments Commission, PO Box 4000 GIPPSLAND MAIL CENTRE VIC 3841

Dear Sir/Madam

### Re: Change to Company Details & Notification of New Shares Issue

Please find enclosed Form 484, Section C, with respect to changes in the top 20 members of the company as at 13 November 2003 and also in respect to notification of a new issue of shares by the company (see section C2 of the Form).

We noted that the Annual Company Statement provided by you does not reflect changes we advised you of in ASIC Form 484 sent to your postal address on 22 September 2003. These changes related to the issue of 30,771,540 fully paid ordinary shares with an issue price of 13 cents per share and the issue of 900 fully paid ordinary shares with an issue price of 20 cents per share. We would appreciate you amending your records to reflect these changes. We have attached reconciliations of the issued shares and total amount paid on these shares as reflected in the Annual Company Statement dated 13 November 2003 to the actual current balances which are reflected in our records.

Please do not hesitate to contact me if you have any questions. We would be pleased if you would acknowledge receipt of this letter and its attachments in due course.

Yours faithfully

Natalie Korchev

N. Korchar

**Company Secretary** 

Encl

Please Note: The new contact numbers for Antisense Therapeutics are now: Phone: 9827 8999 Fax: 9827 1166 16 December 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

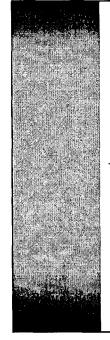
Re: Updated Corporate Presentation

Please find attached Antisense Therapeutics Limited's updated company presentation.

The attached presentation includes an update on our pipeline research projects and information regarding our investigation of the application of ATL1101 (currently being developed for psoriasis) in other skin disease indications.

Yours sincerely

Natalie Korchev Company Secretary





### Antisense Therapeutics Limited

(ASX: ANP)

December 2003

### nse Therapeutics

### Antisense Therapeutics Ltd

- ♦ Listed on ASX Dec 2001
- ♦ Total funds raised to date: \$28.5 M
- ♦ Market Cap: A\$46.2 M
- ♦ Key Shareholders
  - Circadian 20%
  - Syngene 15% (42% Circadian)
  - Isis 11%
  - QIC 5%
- ♦ Cash reserves of A\$15.9 M, no borrowings

## tisense Therapeutics

### **Board of Directors**

- ♦ Bob Moses, Chairman (ex VP of CSL)
- ♦ Mark Diamond, CEO (ex Faulding)
- ♦ Dr Chris Belyea (CEO Metabolic)
- ◆ Dr Stanley Crooke (Founder ISIS Pharmaceuticals, Inc)
- ◆ Prof Graham Mitchell (Foursight/CSL)
- ♦ Prof George Werther (MCRI)

## isense Therapeutics

### ANP's Mission

Create, develop and commercialize novel antisense pharmaceuticals for large unmet markets.



### Business strategy

- ◆ Leverage 14 years of Isis antisense technology development
- ◆ Fast track existing lead projects through pre-clinical and clinical development
- ◆ Create pipeline of new antisense therapeutics
- ◆ Commercialise those that are successful in clinical testing via licensing/partnering

## Antisense Therapeutics

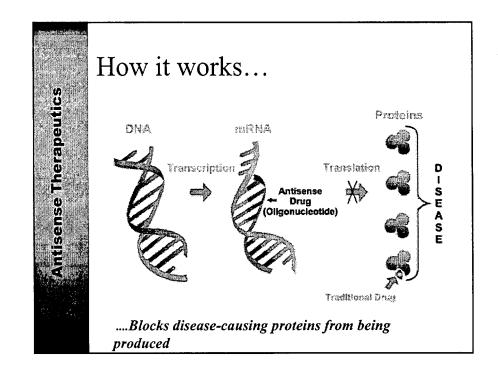
### Strategic Partner ISIS Pharmaceuticals Inc

- ♦ Acknowledged global leader in antisense
- ◆ Over US \$1B invested in antisense chemistries
- ♦ More than 1,000 patents issued
- ♦ 1 FDA drug approved, 8 in late stage clinical development
- ◆ Deals with large market cap companies (eg Lilly and Amgen)



### What is antisense technology?

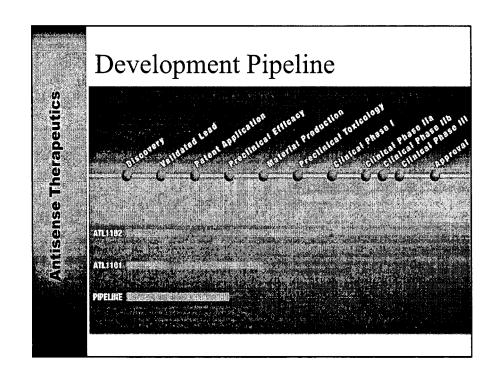
- A fundamentally different approach to making medicine:
- ♦ Unprecedented target specificity and selectivity
- ♦ Most current drugs interfere with the activity of proteins that cause disease
- ♦ Antisense drugs go to work earlier, they block the manufacture of the target protein





### Technical advantages

- ◆ Mature technology (20 years in development)
- ♦ Drug discovery and research is faster and more predictable
- ◆ Compounds are potentially more selective, effective and less toxic
- ♦ Broad disease application
- ♦ Dosing advantages (route and frequency)



## **Antisense Therapeutics**

### Multiple Sclerosis - ATL1102

### ♦ Disease & Market

- Life-long chronic disease of the central nervous system
- Global drug sales of > US\$2.5bn in 2002
- Need for more effective drug with less side effects

### ♦ Product

- Antisense inhibitor to VLA-4 protein which contributes to onset of disease
- Biogen monoclonal ab to VLA-4 in Phase III
- Anticipate efficacy, dosing and cost advantages

## isense Therapeutics

### Multiple Sclerosis - ATL1102 (cont)

### ◆ Progress

- Confirmed activity in pre-clinical murine models of MS also in arthritis and asthma models
- Manufactured drug product for Phase I and IIa studies
- Phase I human trial underway dosing completed

### ♦ Outlook

Following successful completion of Phase I trial, Phase IIa trials in 2<sup>nd</sup> half 2004

## Antisense Therapeutics

### Psoriasis Treatment - ATL1101

- ♦ Disease & Market
  - Chronic non-contagious skin disorder
  - Affects 1-2% of population
  - Global drug sales forecast to exceed US\$2 billion by 2007 (Frost & Sullivan)
  - Need for more effective therapies
- **♦** Product
  - Antisense inhibitor to IGF-IR regulates cell growth
  - Developing topical formulation

## ntisense Therapeutics

### Psoriasis Treatment - ATL1101(cont)

- ◆ Progress
  - Completed pre-clinical efficacy program
  - Awarded A\$1.1 million government grant
  - "Proof of Concept" (PoC) study in psoriasis patients
    - Manufacture of compound for study underway
    - Contracted commercial laboratory to conduct animal toxicology program

## Antisense Therapeutics

### Psoriasis Treatment - ATL1101(cont)

- ♦ Outlook
  - Commence PoC trial in 2<sup>nd</sup> half 2004 after toxicology studies completed and relevant approvals received
  - Investigating ATL1101 in other skin indications: seborrhoeic keratosis and keloid scarring

## ntisense Therapeutics

### Research Pipeline

- ◆ Projects that target diseases of growth, vision and major auto-immune diseases
- ♦ Animal studies are at various stages of completion
- ◆ Positive results in animal studies for most advanced research pipeline project:
  - Results comparable to leading therapy; same animal model for the same disease indication
  - Patent applications filed
  - Follow up animal studies to be completed 1Q'04

<u> </u>	Outloc	ok	
	Project	Value Driver	Timing
Therapeutics	ATL1102 (MS)	◆ Complete Phase I  ◆ Start Phase IIa  ◆ Partnering objective	1 <sup>st</sup> half '04 2 <sup>nd</sup> half '04 Concl Ph IIa
Antisense Thera	ATL1101 (Psoriasis)	◆ Complete product manufacture and toxicology program  ◆ Start "Proof of Concept" study  ◆ Partnering objective	1st half '04  2nd half '04  Concl "PoC"
A	Pipeline Research	◆ Complete multiple animal studies with new antisense leads ◆ Objective: to partner a compound at pre-clinical stage	Ongoing By end 2005

## itisense Therapeutics

### Summary

- ♦ Significant progress in R&D activities
- ♦ Strong cash position allowing ANP to fund key milestones on lead projects
- ◆ Effective leveraging of partnerships to expedite R&D programs and reduce development cost and risk
- ♦ Clear commercialisation objectives

High growth potential/reduced technical risk



22 December 2003

The Companies Section
Announcements
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Application for Quotation of Securities (Appendix 3B)
End of Restriction Period

We refer to the 133,312,508 fully paid ordinary shares of Antisense Therapeutics Limited whose restriction period ended on 19 December 2003 and attach an Application for Quotation of Additional Securities (Appendix 3B).

Yours faithfully

Natalie Korchev Company Secretary

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

### Appendix 3B

### New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002.

Name of entity

Antisense Therapeutics Limited

ABN_		
41 0	95 060 745	
We	(the entity) give ASX the following	ng information.
	rt 1 - All issues nust complete the relevant sections (attach sh	neets if there is not enough space).
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	N/A
2	Number of *securities issued or to be issued (if known) or maximum number which may be issued	N/A
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	N/A

11/3/2002 Appendix 3B Page 1

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?  If the additional securities do not rank equally, please state:  • the date from which they do • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
5	Issue price or consideration	N/A	
	•		
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	N/A	
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	N/A	
			CI
_		Number	+Class
8	Number and *class of all *securities quoted on ASX (including the securities in clause 2 if applicable)	N/A	N/A

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

		Number	+Class
9	Number and *class of all *securities not quoted on ASX (including the securities in clause 2 if applicable)	N/A	N/A
10	Dividend policy (in the case of a trust, distribution policy) on the increased capital (interests)	N/A	
Part	2 - Bonus issue or pro	o rata issue	
11	Is security holder approval required?	N/A	
12	Is the issue renounceable or non-renounceable?	N/A	
13	Ratio in which the *securities will be offered	N/A	
14	*Class of *securities to which the offer relates	N/A	
15	<sup>+</sup> Record date to determine entitlements	N/A	
16	Will holdings on different registers (or subregisters) be aggregated for calculating entitlements?		
17	Policy for deciding entitlements in relation to fractions	N/A	
18	Names of countries in which the entity has *security holders who will not be sent new issue documents		
	Note: Security holders must be told how their entitlements are to be dealt with.  Cross reference: rule 7.7.		
19	Closing date for receipt of acceptances or renunciations	N/A	

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a broker and accept for the balance?	N/A
32	How do *security holders dispose of their entitlements (except by sale through a broker)?	N/A

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

33	<sup>+</sup> Despatch date	N/A
	rt 3 - Quotation of sec	
34	Type of securities (tick one)	
(a)	Securities described in Par	1
(b)		he end of the escrowed period, partly paid securities that become fully paid, ties when restriction ends, securities issued on expiry or conversion of
Ent	ities that have ticked box	34(a)
	litional securities forming a new e additional securities do not form a new	
Tick docur	to indicate you are providing the inj ments	formation or
35		quity securities, the names of the 20 largest holders of the d the number and percentage of additional *securities held by
36		equity securities, a distribution schedule of the additional anumber of holders in the categories
37	A copy of any trust deed	for the additional *securities
(now	go 10 43)	

<sup>+</sup> See chapter 19 for defined terms.

#### Entities that have ticked box 34(b)

Number of securities for which quotation is sought

133,312,508

39 Class of \*securities for which quotation is sought

Fully paid ordinary shares

Do the \*securities rank equally in all respects from the date of allotment with an existing \*class of quoted \*securities?

\*securities?

If the additional securities do not rank equally, please state:

- the date from which they do
- the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment
- the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment
- 41 Reason for request for quotation now

Example: In the case of restricted securities, end of restriction period

(if issued upon conversion of another security, clearly identify that other security)

End of restriction period.

42 Number and \*class of all \*securities quoted on ASX (including the securities in clause 38)

Number	+Class
355,253,350 91,467,765	Ordinary Shares (ANP) Options (ANPO)

(now go to 43)

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

#### All entities

#### Fees

43

Paym	ent method (tick one)
	Cheque attached
	Electronic payment made
	Electronic payment made  Note: Payment may be made electronically if Appendix 3B is given to ASX electronically at the same time.
<b>✓</b>	Periodic payment as agreed with the home branch has been arranged  Note: Arrangements can be made for employee incentive schemes that involve frequent issues of securities.

#### Quotation agreement

- <sup>†</sup>Quotation of our additional \*securities is in ASX's absolute discretion. ASX may quote the \*securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the +securities to be quoted, it has been provided at the time that we request that the +securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

11/3/2002

Appendix 3B Page 7

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before 'quotation of the 'securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here: Natalie Korchev Date: 22 December 2003

Company secretary

Print name: Natalie Korchev

== == == == ==

<sup>+</sup> See chapter 19 for defined terms.

24 December 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Appendix 3Y - Change of Director's Interest Notice

Please find enclosed a Change of Director's Interest Notice for Robert W Moses.

Yours sincerely

Natalie Korchev Company Secretary

Rule 3.19A.2

## Appendix 3Y

### **Change of Director's Interest Notice**

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 30/9/2001.

Name of entity:	Antisense Therapeutics Limited	
ABN:	41 095 060 745	

We (the entity) give ASX the following information under listing rule 3.19A.2 and as agent for the director for the purposes of section 205G of the Corporations Act.

Name of Director	Robert W Moses
Date of last notice	14 October 2003

#### Part 1 - Change of director's relevant interests in securities

In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Note: In the case of a company, interests which come within paragraph (i) of the definition of "notifiable interest of a director" should be disclosed in this part.

Direct or indirect interest	Indirect	
Nature of indirect interest (including registered holder) Note: Provide details of the circumstances giving rise to the relevant interest.	Mrs Lorraine Sandra Moses, wife of Robert Moses, non-executive chairman of Antisense Therapeutics Limited, purchased ordinary shares in Antisense Therapeutics Limited.	
Date of change	22 December 2003	
No. of securities held prior to change	288,462 ordinary shares fully paid 125,000 options expiring 1/2/07 exercisable at 20 cents each 250,000 options expiring 31/7/05 exercisable at 20 cents each	
Class	Fully paid ordinary shares	
Number acquired	100,000	
Number disposed	•	
Value/Consideration  Note: If consideration is non-cash, provide details and estimated valuation	\$13,000 (i.e. 13 cents per share)	

<sup>+</sup> See chapter 19 for defined terms.

11/3/2002 Appendix 3Y Page 1

No. of securities held after change	388,462 125,000	ordinary shares fully paid options expiring 1/2/07 exercisable at 20 cents each
	250,000	options expiring 31/7/05 exercisable at 20 cents each
Nature of change Example: on-market trade, off-market trade, exercise of options, issue of securities under dividend reinvestment plan, participation in buy-back	On-market	trade

#### Part 2 – Change of director's interests in contracts

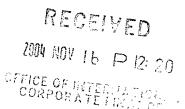
Note: In the case of a company, interests which come within paragraph (ii) of the definition of "notifiable interest of a director" should be disclosed in this part.

N/A
N/A

Appendix 3Y Page 2 11/3/2002

<sup>+</sup> See chapter 19 for defined terms.





14 January 2004

## Antisense Therapeutics CEO Mark Diamond to be Featured Guest on Biotech Today Radio Program

On Wednesday 14 January at 4.20pm United States EST (8.20 am Thursday 15 January Australia EST), Antisense Therapeutics CEO, Mark Diamond, will appear as a featured guest on *Biotech Today*, a U.S. internet radio forum focusing on biotechnology, nanotechnology, pharma, and biomedicine. The live and archived broadcast can be accessed at the following Internet link: www.biotechtoday.net

On the program, Mr. Diamond will discuss the Company's mission, business model, market opportunity and lead compounds which target Multiple Sclerosis and Psoriasis.

Through its strategic partnership with Isis Pharmaceuticals (Nasdaq: ISIS), Antisense Therapeutics has access to Isis's most advanced 2<sup>nd</sup> generation antisense chemistry for selection, development and commercialisation.

Antisense Therapeutics is currently undertaking a Phase I clinical trial of ATL1102 for Multiple Sclerosis. ATL1102 is an antisense inhibitor of VLA-4 (Very Late Antigen-4). Inhibition of VLA-4 has been shown to have positive effects in multiple animal models of inflammatory diseases, including MS.

#### About Antisense Therapeutics Limited

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company. Antisense Therapeutics' mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

Antisense Therapeutics plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

The Company's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Further company details are available on the Antisense Therapeutics website: www.antisense.com.au

#### **Contact Information:**

CEO – Antisense Therapeutics Ltd. - Mark Diamond +61-3-9827-8999

Company Secretary – Antisense Therapeutics Ltd. - Natalie Korchev +61-3-9827-8999

Media Information – Rebecca Christie or Kate Mazoudier – Buchan Communications Group - +61-3-9866-4722

30 January 2004

The Companies Section
Announcements
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

## ATL1102 Preliminary Phase I results - presentation at Neurosciences Conference

As announced in the company's Investor Update dated 9 December 2003, dosing is completed in both single and multiple dose Phase 1 human clinical trials on ATL1102, Antisense Therapeutics second generation antisense drug for multiple sclerosis (MS).

The aims of the Phase 1 trials are to obtain information on the pharmacokinetic<sup>1</sup> behaviour of ATL1102 in humans and to assess the safety and tolerability of increasing dose levels of ATL1102.

Some preliminary data from these clinical trials are being presented at the Australian Neuroscience Society Scientific Conference in Melbourne today.

Blood and other biological samples are being collected from every individual to measure safety parameters and the blood level concentrations of the delivered drug and safety parameters over prolonged periods of time (lasting several months after dosing). Laboratory analyses and collection of the biological samples are still continuing and full and final results are expected to be reported mid-year.

Preliminary indications from the data collected and analysed so far are favourable for both safety and pharmacokinetics.

These indications provide Antisense Therapeutics with the confidence to begin planning the Phase IIa clinical trials in MS patients with the selection of appropriate dose levels and dosing regimens. At present, study designs for the Phase IIa clinical trial are being discussed with potential clinical trialists and contract organisations.

Once final reports are received for the Phase I trial and the results are assessed as satisfactory, the company will make an application for the Phase IIa patient trial.

<sup>&</sup>lt;sup>1</sup> "Pharmacokinetics" is how the drug distributes in the body over time after administration, helpful in deciding dosing frequency in future studies

Regulatory agency approval and commencement of the Phase IIa trial are targeted for the second half of 2004.

A copy of the PowerPoint presentation made to the Australian Neurosciences Conference is available on the Antisense Therapeutics website <a href="www.antisense.com.au">www.antisense.com.au</a>.

#### **Background Information**

Multiple Sclerosis (MS) is a life-long chronic, incurable disease that progressively destroys the central nervous system. It is commonly diagnosed between the ages of 20 and 40 years. MS affects about 350,000 people in the US where the estimated cost of the disease is more than US\$2.5 billion. Although current treatments are unable to slow disease progression, the aims of therapy are to reduce the duration, frequency and severity of attacks.

ATL1102 is a drug under development by Antisense Therapeutics, which aims to prevent the synthesis of a protein called VLA-4 known to play a part in both the onset and progression of MS.

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company (ASX: ANP). ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101). ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies. The company's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Further company details are available on the Antisense Therapeutics website.

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999 CFFICE OF INTERMATING

Rule 4.7B

## **Appendix 4C**

# Quarterly report for entities admitted on the basis of commitments

Introduced 31/3/2000. Amended 30/9/2001

ANTISENSE THERAPEUTICS LIMITED	
ABN	Quarter ended ("current quarter")

41 095 060 745 31 DECEMBER 2003

#### Consolidated statement of cash flows

Cash	flows related to operating activities	Current quarter	Year to date (6 months)
		\$A'000	\$A'000
1.1	Receipts from customers	242	703
1.2	Payments for (a) staff costs	(348)	(718)
	(b) advertising and r	<u> </u>	
	(c) research and dev	elopment (474)	(1,172)
	(d) leased assets	-	
	(e) other working ca	pital * (83)	(266)
1.3	Dividends received	-	
1.4	Interest and other items of a sim received	ilar nature 160	262
1.5	Interest and other costs of finance paid	-	
1.6	Income taxes paid	-	
1.7	Other (provide details if material) - Income Tax refund	(3)	372
	Net operating cash flows	(506)	(819)

<sup>\*</sup> Includes GST paid to suppliers and GST credits received from ATO.

<sup>+</sup> See chapter 19 for defined terms.

		Current quarter \$A'000	Year to date (6 months) \$A'000
1.8	Net operating cash flows (carried forward)	(506)	(819)
	Cash flows related to investing activities		
1.9	Payment for acquisition of:		-
	(a) businesses (item 5)	-	-
	(b) equity investments	-	-
	(c) intellectual property (d) physical non-current assets	(8)	(8)
	(e) other non-current assets	-	(0)
1.10	Proceeds from disposal of:		
	(a) businesses (item 5)	-	-
	(b) equity investments	-	•
	(c) intellectual	-	•
	property (d) physical non-	- 1	
	current assets	_	
	(e) other non-current assets	-	•
1.11	Loans to other entities	-	
1.12	Loans repaid by other entities	-	•
1.13	Other (provide details if material)	-	•
	Net investing cash flows	(8)	(8)
1.14	Total operating and investing cash flows	(514)	(827)
	Cash flows related to financing activities		
1.15	Proceeds from issues of shares, options, etc.	6,396	10,396
1.16	Proceeds from sale of forfeited shares		,
1.17	Proceeds from borrowings		
1.18	Repayment of borrowings	j	
1.19	Dividends paid		
1.20	Other - costs relating to issue of shares	(106)	(294)
	Net financing cash flows	6,290	10,102
	Net increase (decrease) in cash held	5,776	9,275
1.21	Cash at beginning of quarter/year to date	10,045	6,546
1.22	Exchange rate adjustments to item 1.20	-	
1.23	Cash at end of quarter	15,821	15,82

Appendix 4C Page 2 30/9/2001

<sup>+</sup> See chapter 19 for defined terms.

## Payments to directors of the entity and associates of the directors Payments to related entities of the entity and associates of the related entities

		Current quarter \$A'000
1.24	Aggregate amount of payments to the parties included in item 1.2	322
1.25	Aggregate amount of loans to the parties included in item 1.11	•

1.26 Explanation necessary for an understanding of the transactions

Item 1.24 Reflects the following related party payments:

- (a) Total amounts paid to directors include director's fees, salaries and superannuation of \$106,151 (YTD: \$231,368).
- (b) Dr Stanley Crooke, a director of the Company is also a director of Isis Pharmaceuticals Inc ("Isis"). A total amount of \$77,709 (YTD: \$186,703) was paid to Isis for research and development related services provided by them to Antisense Therapeutics Limited ("ATL").
- (c) Professor George Werther, a director of the company, is an executive officer of the Murdoch Childrens Research Institute ("MCRI"). An amount of \$138,593 (YTD: \$367,663) was paid to the MCRI for research services performed by them for ATL.

#### Non-cash financing and investing activities

2.1	Details of financing and investing transactions which have had a material effect on consolidated
	assets and liabilities but did not involve cash flows

	-	
Not applicable.		

2.2 Details of outlays made by other entities to establish or increase their share in businesses in which the reporting entity has an interest

, , , , , , , , , , , , , , , , , , ,	
Not applicable.	

#### Financing facilities available

Add notes as necessary for an understanding of the position. (See AASB 1026 paragraph 12.2).

		Amount available \$A'000	Amount used \$A'000
3.1	Loan facilities	-	-
3.2	Credit standby arrangements	-	-

<sup>+</sup> See chapter 19 for defined terms.

30/9/2001 Appendix 4C Page 3

#### Reconciliation of cash

Reconciliation of cash at the end of the quarter (as shown in the consolidated statement of cash flows) to the related items in the accounts is as follows.		Current quarter \$A'000	Previous quarter \$A'000
4.1	Cash on hand and at bank	3,321	1,545
4.2	Deposits at call	12,500	8,500
4.3	Bank overdraft	•	-
4.4	Other (provide details)	-	-
	Total: cash at end of quarter (item 1.23)	15,821	10,045

#### Acquisitions and disposals of business entities

		Acquisitions (Item 1.9(a))	Disposals (Item 1.10(a))
5.1	Name of entity	Not applicable	Not applicable
5.2	Place of incorporation or registration		
5.3	Consideration for acquisition or disposal		
5.4	Total net assets		
5.5	Nature of business		

#### Compliance statement

- 1 This statement has been prepared under accounting policies which comply with accounting standards as defined in the Corporations Act (except to the extent that information is not required because of note 2) or other standards acceptable to ASX.
- 2 This statement does give a true and fair view of the matters disclosed.

Sign here:

Natalie Korchev.........

Date: 30 January 2003

Company secretary

Print name:

Natalie Korchev

Appendix 4C Page 4 30/9/2001

<sup>+</sup> See chapter 19 for defined terms.

#### **Notes**

- The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity wanting to disclose additional information is encouraged to do so, in a note or notes attached to this report.
- 2. The definitions in, and provisions of, AASB 1026: Statement of Cash Flows apply to this report except for the paragraphs of the Standard set out below.
  - 6.2 reconciliation of cash flows arising from operating activities to operating profit or loss
  - 9.2 itemised disclosure relating to acquisitions
  - 9.4 itemised disclosure relating to disposals
  - 12.1(a) policy for classification of cash items
  - 12.3 disclosure of restrictions on use of cash
  - 13.1 comparative information
- 3. Accounting Standards. ASX will accept, for example, the use of International Accounting Standards for foreign entities. If the standards used do not address a topic, the Australian standard on that topic (if any) must be complied with.

30/9/2001 Appendix 4C Page 5

<sup>+</sup> See chapter 19 for defined terms.





12 February 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: HALF-YEAR REPORT (REVIEWED)
31 December 2003

In accordance with Listing Rule 4.2A we enclose the Half-Year Report (Appendix 4D) (reviewed) on the results of Antisense Therapeutics Limited ('Antisense Therapeutics') for the half-year ended 31 December 2003.

#### Results

The Directors report a loss of \$1,626,940 (2002: \$3,882,283) which includes an income tax benefit of \$371,820 (2002: \$nil). The loss is after fully expensing all research and development costs.

The receipt of payments under the R&D Start Grant awarded to the psoriasis project (\$638,700) and the cash rebate received in relation to the Research and Development Tax Concession (\$371,820) have contributed to the reduction in the loss this half-year compared to the same period in 2002. The result also reflects reduced research and development costs this half-year compared to the half-year ended 31 December 2002 as the majority of the costs of the manufacturing, development and formulation of ATL1102 were incurred in the 2002 half-year period.

The company also successfully raised \$10.4 million through share placements during the period.

Antisense Therapeutics has no borrowings and has cash and bank term deposits as at 11 February 2004 amounting to \$15.3 million.

#### Key Highlights

(To be read in conjunction with the Directors' Report which contains a detailed report on the company's operations as contained in the Half-Year Report attached)

During the period under review the company has focused on meeting the key project milestones for its lead compounds, ATL1102 for multiple sclerosis and ATL1101 for psoriasis. Progress has also been made in other research projects. The major achievements of the company were:

#### Multiple Sclerosis Project (ATL1102)

 Commencement and completion of single and multiple dosing of volunteers in the Phase I human trials.  Presentation of preliminary Phase I trial results at the Australian Neurosciences Society Conference, on 30 January 2004, which indicate that the data collected and analysed so far are favourable for both safety and pharmacokinetics.

#### Psoriasis Treatment Project (ATL1101)

- Initiation of the human 'proof of concept' study, an accelerated path to testing the activity of ATL1101 in humans suffering psoriasis.
- Completion of the manufacture of the bulk active pharmaceutical ingredient and commencement of formulation of injectable and cream presentations for use in the human 'proof of concept' study.

#### Share Placement

During the period under review, the company raised \$10.4 million through new shares issues. Of this amount \$5 million was raised through a private placement of ordinary shares to Australian institutions and professional investors, and \$5.4 million was raised pursuant to the company's Share Purchase Plan.

Further details regarding the progress of the company's operations are provided in the Directors' Report included in the Half-Year Report attached.

This letter and the attached Half-Year Report form part of this announcement to the Australian Stock Exchange Limited and should be read in conjunction with the company's Annual Report for the year ended 30 June 2003.

Yours faithfully

**Antisense Therapeutics Limited** 

Mark Diamond Managing Director

#### **APPENDIX 4D**

#### Half-Year Report

Name of entity:

ANTISENSE THERAPEUTICS LIMITED

ABN:

41 095 060 745

Reporting period:

HALF YEAR ENDED 31 DECEMBER 2003

Previous

Corresponding period: HALF YEAR ENDED 31 DECEMBER 2002

#### **INDEX**

- 1. Results for announcement to the market
- 2. Financial Report
  - Independent Review Report
  - Directors' Report
  - Financial Statements
  - Directors' Declaration
- Other Information

#### THIS HALF-YEAR REPORT IS TO BE READ IN CONJUNCTION WITH THE COMPANY'S 2003 ANNUAL REPORT

Note: The financial figures provided are in actual Australian dollars, unless specified otherwise.

#### RESULTS FOR ANNOUNCEMENT TO THE MARKET

The results of Antisense Therapeutics Limited for the half-year ended 31 December 2003 are as follows:

Revenues and Results from Ordinary Activities:		Change compared to half year to 31/12/02 %	Half year to 31/12/03
Revenues from ordinary activities	Up by \$763,529	428%	941,987
Profit (loss) from ordinary activities after tax attributable to members	Loss has decreased by \$2,255,343	58%	(1,626,940)
Net profit (loss) for the period attributable to members	Loss has decreased by \$2,255,343	58%	(1,626,940)

#### Dividends:

No dividends have been paid or declared by the entity since the beginning of the current reporting period.

No dividends were paid for the previous corresponding period.

#### Brief Explanation of figures reported above:

Revenue from ordinary activities increased in the current period due to increased interest income and the receipt of payments under the R&D Start Grant awarded to the psoriasis project.

The loss for the company for the half-year was \$1,626,940 (2002: \$3,882,283) including an income tax benefit of \$371,820 (2002: \$nil). The loss is after fully expensing all research and development costs. The receipt of payments under the R&D Start Grant awarded to the psoriasis project (\$638,700) and the cash rebate received in relation to the Research and Development Tax Concession (\$371,820) have contributed to the reduction in the loss this half-year compared to the same period in 2002. The result also reflects reduced research and development costs this half-year compared to the half-year ended 31 December 2002 as the majority of the costs of the manufacturing, development and formulation of ATL1102 were incurred in the 2002 half-year period.

For further details relating to the current period's results, refer to the company's Directors' Report contained within the Financial Report for the half-year ended 31 December 2003.

#### **Antisense Therapeutics Limited**

ABN 41 095 060 745

Half-Year Financial Report for the half-year 31 December 2003



■ 120 Collins Street Melbourne VIC 3000 Australia

> GPO Box 678 Melbourne VIC 3001

Fax 61.3 9288 8000 Fax 61.3 9654 6166 DX 293 Melbourne

## Independent review report to members of Antisense Therapeutics Limited

#### Scope

The financial report and directors' responsibility

The financial report comprises the statement of financial position, statement of financial performance, statement of cash flows, accompanying notes to the financial statements, and the directors' declaration for Antisense Therapeutics Limited, for the half-year ended 31 December 2003.

The directors of the company are responsible for preparing a financial report that gives a true and fair view of the financial position and performance of the company, and that complies with Accounting Standard AASB 1029 "Interim Financial Reporting", in accordance with the *Corporations Act 2001*. This includes responsibility for the maintenance of adequate accounting records and internal controls that are designed to prevent and detect fraud and error, and for the accounting policies and accounting estimates inherent in the financial report.

#### Review approach

We conducted an independent review of the financial report in order to make a statement about it to the members of the company, and in order for the company to lodge the financial report with the Australian Stock Exchange and the Australian Securities and Investments Commission.

Our review was conducted in accordance with Australian Auditing Standards applicable to review engagements, in order to state whether, on the basis of the procedures described, anything has come to our attention that would indicate that the financial report is not presented fairly in accordance with the *Corporations Act 2001*, Accounting Standard AASB 1029 "Interim Financial Reporting" and other mandatory professional reporting requirements in Australia and statutory requirements, so as to present a view which is consistent with our understanding of the company's financial position, and of its performance as represented by the results of its operations and cash flows.

A review is limited primarily to inquiries of company personnel and analytical procedures applied to the financial data. These procedures do not provide all the evidence that would be required in an audit, thus the level of assurance is less than given in an audit. We have not performed an audit and, accordingly, we do not express an audit opinion.

#### Independence

We are independent of the company, and have met the independence requirements of Australian professional ethical pronouncements and the *Corporations Act 2001*. In addition to our review of the financial report, we were engaged to undertake the services disclosed in the notes to the financial statements. The provision of these services has not impaired our independence.

#### Statement

Based on our review, which is not an audit, we have not become aware of any matter that makes us believe that the financial report of Antisense Therapeutics Limited is not in accordance with:

- (a) the Corporations Act 2001, including:
  - (i) giving a true and fair view of the financial position of Antisense Therapeutics Limited at 31 December 2003 and of its performance for the half-year ended on that date; and
  - (ii) complying with Accounting Standard AASB 1029 "Interim Financial Reporting" and the *Corporations Regulations 2001*; and
- (b) other mandatory financial reporting requirements in Australia.

Ernst & Young

Denis Thon

Erust & Young

Denis Thorn Partner

Melbourne

12 February 2004

#### ANTISENSE THERAPEUTICS LIMITED

ABN 41 095 060 745

#### **DIRECTORS' REPORT**

The Board of Directors of Antisense Therapeutics Limited ("ATL" or "company") has pleasure in submitting its report in respect of the financial half-year ended 31 December 2003.

#### **Directors**

The names of the directors in office during or since the end of the half-year are:

Mr Robert W Moses (Chairman)
Mr Mark Diamond (Managing Director)
Dr Chris Belyea
Dr Stanley Crooke
Prof Graham Mitchell
Prof George Werther

Unless otherwise indicated, all directors held their position as a director throughout the entire half-year and up to the date of this report.

#### **Principal Activities**

The principal activity of the company is to apply the best in antisense technology (by utilising industry alliances and the company's growing expertise in the field) to develop therapeutics for commercially important human conditions.

#### **Results and Review of Operations**

During the period under review Antisense Therapeutics Limited has progressed its most advanced projects in the following disease areas:

- (a) multiple sclerosis (ATL1102); and
- (b) psoriasis (ATL1101).

#### Results

The loss for the company for the half-year was \$1,626,940 (2002: \$3,882,283) including an income tax benefit of \$371,820 (2002: \$nil). The loss is after fully expensing all research and development costs. The receipt of payments under the R&D Start Grant awarded to the psoriasis project (\$638,700) and the cash rebate received in relation to the Research and Development Tax Concession (\$371,820) have contributed to the reduction in the loss this half-year compared to the same period in 2002. The result also reflects reduced research and development costs this half-year compared to the half-year ended 31 December 2002 as the majority of the costs of the manufacturing, development and formulation of ATL1102 were incurred in the 2002 half-year period.

#### Review of Operations

Detailed below is an update on the progress of the company's projects and overall operations for the half-year ended 31 December 2003.

Antisense Therapeutics Limited's 30 June 2003 annual report contains background information relating to its research and development projects and collaboration partners/agreements. ATL's 30 June 2003 annual report should be read in conjunction with this report.

#### Multiple Sclerosis (ATL1102) Project

ATL1102 is designed to block the synthesis of an immune system component or protein called VLA-4 that is known to play a part in both the onset and progression of multiple sclerosis ("MS").

In August 2003, the company commenced Phase I human clinical trials of ATL1102 at the Charterhouse Clinical Research Unit in London.

The aims of these Phase I trials are to obtain information on the pharmacokinetic behaviour of ATL1102 in humans and to assess the safety and tolerability of increasing dose levels of ATL1102 injected as single and multiple doses. Fifty-four healthy volunteers have participated in the placebo-controlled, randomised, double-blind study.

The study has progressed rapidly, having completed both single and multiple dosing schedules.

Laboratory investigations of the biological samples collected during the trial are currently taking place. Some preliminary data from these clinical trials were presented at the Australian Neuroscience Society Scientific Conference in Melbourne on 30 January 2004. As reported by the company on that date, preliminary indications from the data collected and analysed so far are favourable for both safety and pharmacokinetics.

These indications provide the company with the confidence to begin planning the Phase IIa clinical trials in MS patients with the selection of appropriate dose levels and dosing regimens. At present, study designs for the Phase IIa clinical trial are being discussed with potential clinical trialists and contract organisations.

#### Outlook

Once final reports are received for the Phase I trial and the results are assessed as satisfactory, the company will make an application for the Phase IIa patient trial.

Regulatory agency approval and commencement of the Phase IIa trial are targeted for the second half of 2004.

#### Psoriasis (ATL1101) Project

ATL1101 is designed to block the synthesis of the IGF-1 receptor, a protein involved in the regulation of cell growth in psoriasis.

In July 2003, the company announced its plans to undertake a "proof of concept" study, which is an accelerated path to testing the activity of ATL1101 in humans suffering psoriasis. In this "proof of concept" study, also referred to as the small plaque assay (SPA), a relatively small quantity of ATL1101 will be applied to areas of psoriatic skin on a limited number of patients.

The human study is to commence once supplies of drug product are manufactured and a limited animal toxicology program is performed. The manufacture of the active pharmaceutical ingredient and the analytical work required for product release was completed during the half-year ended 31 December 2003 and the formulation of injectable and cream presentations of ATL1101 is currently underway.

The psoriasis project is supported by a Commonwealth Government R&D Start grant of A\$1.1 million.

#### **Outlook**

The limited animal toxicology studies are scheduled to commence in mid 2004 following completion of the formulation activities. Subject to receiving the relevant approvals to conduct the study, the human "proof of concept" study is expected to begin in the second half of 2004.

<sup>&</sup>lt;sup>1</sup> "Pharmacokinetics" is how the drug distributes in the body over time after administration, helpful in deciding dosing frequency in future studies.

#### Other Projects

Currently, the company has research projects involving new drugs that target diseases of growth, vision and several major auto-immune diseases. These animal studies are at various stages of completion.

During the period under review, the company has produced positive results in an experimental system in mice for a second-generation antisense compound. These results have confirmed the potential of the antisense treatment for its given disease indications. The company expects to provide further details of the results of this research project in due course.

#### Share Placement

During the period under review, the company raised \$10.4 million through new shares issues. Of this amount \$5 million was raised through a private share placement to Australian institutions and professional investors, with the issue of 38.5 million ordinary shares at \$0.13 per share and \$5.4 million was raised pursuant to the company's Share Purchase Plan with the issue of 41.5 million ordinary shares to eligible shareholders at the same price per share.

#### Biotechnology Companies - Inherent Risks

Some of the risks inherent in the development of a product to a marketable stage include the uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of the necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Also a particular compound may fail the clinical development process through lack of efficacy or safety. Companies such as Antisense Therapeutics Limited are dependent on the success of their research projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in these areas must be regarded as speculative taking into account these considerations.

This annual report may contain forward-looking statements regarding the potential of the company's projects and interests and the development and therapeutic potential of the company's research and development. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercialising drugs that are safe and effective for use as human therapeutics and the financing of such activities. There is no guarantee that the company's research and development projects will be successful or receive regulatory approvals or prove to be commercially successful in the future. Actual results of further research could differ from those projected or detailed in this report. As a result, you are cautioned not to rely on forward-looking statements. Consideration should be given to these and other risks concerning the company's research and development program referred to in this report for the period ended 31 December 2003.

For and on behalf of the Board:

Chausal

Mark Diamond Director

Melbourne 12 February 2004 Robert Moses Director

## Antisense Therapeutics Limited ABN 41 095 060 745

#### Condensed Statement of Financial Position Half-Year Ended 31 December 2003

	December 2003 \$	June 2003 \$
Current Assets	·	
Cash assets	15,821,358	6,545,567
Receivables	73,820	68,730
Other	616,075	878,941
Total Current Assets	16,511,253	7,493,238
Non-Current Assets		
Plant and equipment	50,022	50,911
Intangible assets	3,794,000	4,438,000
Total Non-Current Assets	3,844,022	4,488,911
Total Assets	20,355,275	11,982,149
Current Liabilities		
Payables	207,453	326,302
Provisions	32,535	38,101
Total Current Liabilities	239,988	364,403
Total Liabilities	239,988	364,403
Net Assets	20,115,287	11,617,746
Equity		
Contributed equity	33,838,985	23,714,504
Reserves	725,885	725,885
Accumulated losses	(14,449,583)	(12,822,643)
Total Equity	20,115,287	11,617,746

### Antisense Therapeutics Limited ABN 41 095 060 745

#### Condensed Statement of Financial Performance Half-Year Ended 31 December 2003

		31 December 2003 \$	31 December 2002 \$
Revenue from ordinary activities	2	941,987	178,458
Administrative expenses Occupancy expenses Patent expenses Research and development expenses		(567,368) (25,615) (2,295) (1,701,469)	(485,268) (22,696) (2,679) (2,906,098)
Research and development expenses - amortisation of intellectual property		(644,000)	(644,000)
Loss from ordinary activities before income tax benefit		(1,998,760)	(3,882,283)
Income tax benefit relating to ordinary activities	3	371,820	
Loss from ordinary activities after related income tax benefit		(1,626,940)	(3,882,283)
Net loss		(1,626,940)	(3,882,283)
Net loss attributable to members of Antisense Therapeutics Limited		(1,626,940)	(3,882,283)
Share issue costs		(271,899)	(271,220)
Total revenues, expenses and valuation adjustments attributable to members of Antisense Therapeutics Limited and recognised directly in equity		(271,899)	(271,220)
Total changes in equity other than those resulting from transactions with owners as owners		(1,898,839)	(4,153,503)
Basic earnings per share (cents per share)		(0.51)	(1.75)
Diluted earnings per share (cents per share)		(0.51)	(1.75)

The accompanying notes form an integral part of this statement of financial performance.

## Antisense Therapeutics Limited ABN 41 095 060 745

#### <u>Condensed Statement of Cash Flows</u> <u>Half-Year Ended 31 December 2003</u>

	31 December 2003	31 December 2002
	\$	\$
Cash Flows from Operating Activities		
Payments to suppliers, employees and for research		
and development	(2,155,718)	(3,680,722)
R&D Start Grant received	702,570	•
Interest received	262,259	194,857
Income tax benefits received	371,974	-
Net cash flows used in operating activities	(818,915)	(3,485,865)
Cash Flows from Investing Activities		
Purchase of plant and equipment	(7,888)	(6,932)
Net cash flows used in investing activities	(7,888)	(6,932)
Cash Flows from Financing Activities		
Proceeds from issue of shares and options	10,396,380	4,521,291
Payment of share and option issue cost	(293,786)	(248,421)
Net cash flows from financing activities	10,102,594	4,272,870
Net increase in cash held	9,275,791	780,074
Add opening cash brought forward	6,545,567	9,373,050
Closing cash carried forward	15,821,358	10,153,124

The accompanying notes form an integral part of this statement of cash flows.

### Antisense Therapeutics Limited ABN 41 095 060 745

### Notes to the Half-Year Financial Statements 31 December 2003

#### Note 1. Basis of Preparation of the Half-Year Financial Report

The half-year financial report does not include all notes of the type normally included within the annual financial report and therefore cannot be expected to provide as full an understanding of the financial performance, financial position and financing and investing activities of the company as the full financial report.

The half-year financial report should be read in conjunction with the Annual Financial Report of Antisense Therapeutics Limited as at 30 June 2003. It is also recommended that the half-year financial report be considered together with any public announcements made by Antisense Therapeutics Limited during the half-year ended 31 December 2003 in accordance with its continuous disclosure obligations arising under the Corporations Act 2001.

#### (a) Basis of Accounting

The half-year financial report is a general-purpose financial report, which has been prepared in accordance with the requirements of the Corporations Act 2001, applicable Accounting Standards including AASB 1029 "Interim Financial Reporting" and Urgent Issues Group Consensus Views.

The half-year financial report has been prepared in accordance with historical cost convention.

For the purpose of preparing the half-year financial report, the half-year has been treated as a discrete reporting period.

#### (b) Going Concern Basis of Preparation

This financial report has been prepared on a going concern basis. In common with start-up biotechnology companies:

- the company's operations are subject to considerable risks due primarily to the nature of research, development and commercialisation to be undertaken; and
- the going concern basis assumes that the existing cash reserves and future capital raisings will
  be sufficient to enable the company to successfully execute its existing and future plans.

The financial statements take no account of the consequences, if any, of the effects of unsuccessful product development or commercialisation nor of the inability of the company to obtain adequate funding. The ability of the company to realise the carrying value of the intangible asset is subject to successful operation of the company's existing and future plans.

		31 December 2003 \$	31 December 2002 \$
Note 2.	Revenues and Expenses from Ordinal	ry Activities	
Revenues	from ordinary activities:		
Interest fro	om external parties	291,301	179,208
Start grant	income	638,700	-
Foreign ex	change gains/(losses):		
Realise	ed	12,386	(33,552)
Unreali	sed	(400)	32,802
Total reve	nues from ordinary activities	941,987	178,458

#### Note 2. Revenues and Expenses from Ordinary Activities (continued)

	31 December 2003 \$	31 December 2002 \$
Expenses and Losses:		
Depreciation of:		
- Equipment and furniture	10,533	9,026
Operating lease rentals:		
Minimum lease payments	20,079	19,494
Amortisation of intangibles	644,000	644,000

#### Note 3. Income Tax Benefit

The income tax benefit comprises cash rebate received during the period in relation to the year ended 30 June 2002 which is available under the Research and Development Tax Concession of the Income Tax Assessment Act 1936.

Note 4.	Contributed Equi	4.,
Note 4.	Contributed Edui	Į٧

	6 months to	12 months to
	31 December	30 June 2003
	2003	
	\$	\$
Contributed equity at beginning of the		
period	23,714,504	19,470,572
Shares issued during the period (i)	10,396,000	4,520,645
Transaction costs arising on share issue	(271,899)	(277,359)
Options exercised during the period	380	646
Contributed equity at end of period	33,838,985	23,714,504
(a) Movement in Contributed Equity		
for the period:	No.	No.
Balance of number of shares at		
beginning of period	275,281,608	215,003,110
Shares issued during the period (i)	79,969,842	60,275,268
Options exercised during the period	1,900	3,230
Balance of number of issued shares at		
end of period	355,253,350	275,281,608

- (i) The following shares were issued during the period:
  - 30,771,540 fully paid ordinary shares at 13 cents per share in a placement of shares to Australian
    institutions and professional investors,
  - 41,508,302 fully paid ordinary shares at 13 cents per share to eligible shareholders pursuant to the company's share purchase plan, and
  - 7,690,000 fully paid ordinary shares at 13 cents per share to Polychip Pharmaceuticals Pty Ltd.

#### Note 5. Subsequent Events

Subsequent to 31 December 2003, there has been no event that has significantly or may significantly affect the operations of the company, the results of those operations or the state of affairs of the company in subsequent financial years.

#### Note 6. Segment Information

The consolidated entity operates predominantly in one industry and one geographical segment, those being the health care industry and Australia respectively.

			31 December 2003 \$	30 June 2003 \$	
Note	7.	Commitments	•	•	
(a)	Expenditure commitments relating to research and development are payable as follows				
	Not	later than one year (i)	1,572,394	1,247,678	
		er than one year, but not later	29,372	-	
	than	i five years			
			1,601,766	1,247,678	
	(i)	This amount includes commitments relating to another entity on behalf of the company under agreement allows for the research to be termic commitment reflects estimated costs that the were to be given at period end.	r a 3 year research agreeme nated with six months notice	nt, however, the . Accordingly, the	
(b)	Ope	rating office lease expenditure contracted for	is payable as follows		

82,713

45,087

#### Note 8. Contingent Liabilities & Contingent Assets

Not later than one year

There were no contingent liabilities or contingent assets at 31 December 2003.

#### **Director's Declaration**

In accordance with a resolution of the directors of Antisense Therapeutics Limited, we state that:

In the opinion of the directors:

- (a) the financial statements and notes of the company:
  - give a true and fair view of the financial position as at 31 December 2003 and the performance for the half-year ended on that date of the company; and
  - (ii) comply with Accounting Standard AASB 1029 "Interim Financial Reporting" and the Corporations Regulations 2001; and
- (b) there are reasonable grounds to believe that the company will be able to pay its debts as and when they become due and payable.

On behalf of the Board

Director

Director

Melbourne, 12 February 2004

#### **OTHER INFORMATION**

	Half-year to 31/12/03	Half-year to 31/12/02
NTA backing		
Net tangible asset backing per ordinary security	4.59 cents	3.19 cents
Earnings per share		
Basic earnings per share (cents per share) Diluted earnings per share (cents per share)	(0.51) cents (0.51) cents	(1.75) cents (1.75) cents

#### Status of review of accounts

This Appendix 4D is based on accounts which have been reviewed. The review report is included with the financial report.

street number & name	Antisense Therapeutics Ltd Level 1 10 Wallace Avenue Toorak state/territory Vic postco 42 (03) 9827 8999 (03) 9827 1166 suburb/city  Australian Securities & Investments Commission notification of	RECEIVED 2004 HOV 16 P 12: 2 CORPORATE MASS. CASH, PROC.	REQ-A REQ-P
	Half Yearly Reports  (to be lodged within 75 days of the end of the accounting period)	(ASX Form 1001) Corporations Act 2001 285(2), 286(1), 320	
Disclosing entity Please complete A, B or C.  A  name  A.C.N.  B	a company  Antisense Therapeutics L:  095 060 745  a body (other than a company)		LS
A.R.B.N. (if applicable)  C  name  A.R.S.N.	a registered scheme		REPORTS
from Certification	I certify that the attached documents comprise the half year every other document that is required to be lodged with the	rly reports together with	X RE
· · · · · · · · · · · · · · · · · · ·	This form is to be signed by:  a director or secretary or the equivalent  a director or secretary of the responsible entity acting in that capacity		ARI
A.C.N		capacity Company Secreta:	y
sign here	Small Business (less than 20 employees), please provide an estimate of   Include  The time actually spent reading the instructions, working on the  The time spent by all employees in collecting and providing this	e question and obtaining the information	HALF

hrs

mins



For release: 24 February 2004

## Successful Animal Study Results Demonstrate Potential New Treatment for Growth and Sight Disorders

#### Highlights

- Demonstration of efficacy in pre-clinical animal studies of new antisense compound
- Results to be presented at International Scientific Symposium
- Outcomes comparable to leading therapeutics
- Major disease applications including acromegaly and diabetic retinopathy
- Patent applications lodged
- Development to commence on new compound (ATL1103)

#### Results of Animal Studies

Antisense Therapeutics Limited is pleased to announce that an antisense inhibitor designed to block the Growth Hormone receptor (GHr) gene has produced definitive results in an experimental system in mice. This confirms its potential as a treatment for diseases associated with excessive growth hormone action. These diseases include acromegaly (an abnormal growth disorder of organs, face, hands and feet), diabetic retinopathy and wet agerelated macular degeneration (AMD). The latter disorders are common diseases of the eye and major causes of blindness.

The targeting of GHr with our proprietary antisense compound inhibits growth hormone activity, thereby reducing levels of the hormone insulin-like growth factor-I (IGF-I) in the blood. Acromegalic patients are known to have significantly higher blood IGF-I levels than healthy individuals. Reduction of these levels to normal is accepted by clinical authorities as the primary marker of an effective drug treatment for the disease. In the case of diabetic retinopathy, published clinical studies have shown that treatments producing a reduction in IGF-I levels retarded the progression of the disease in patients.

Antisense Therapeutics' animal studies for the GHr antisense compound were conducted at the University of Queensland by Professor Michael Waters, internationally recognised for his research on GHr and disorders related thereto. These studies demonstrated that the compound significantly reduces blood levels of IGF-I in mice, an effect which, if reproduced in humans, should provide therapeutic benefit to acromegaly patients and potentially to diabetic retinopathy sufferers.

The animal study results are to be presented by Dr George Tachas, Antisense Therapeutics' Director of Drug Discovery, at the International GH-IGF Symposium, Cairns, Queensland on April 19, 2004.

#### Growth and Sight Disorders - Markets, Current Treatments

The most widely used pharmaceutical treatment for acromegaly is the drug octreotide (Sandostatin<sup>TM</sup>), however a significant percentage of patients do not respond to this therapy while other patients experience adverse reactions with this therapy. The latest drug to be approved in Europe and the US for the treatment of acromegaly is pegvisomant (Trovert<sup>TM</sup>, Somavert<sup>TM</sup>). Pegvisomant is effective in a larger percentage of patients than octreotide although it requires more frequent (daily) dosing by injection than the long acting form of octreotide which is surgically implanted (intragluteal). Sales of pegvisomant are projected to reach US\$500M per annum.

The study results for our GHr antisense compound are comparable to those achieved by pegvisomant in an equivalent animal model. Our GHr antisense compound may have important clinical advantages over pegvisomant and octreotide, including more convenient route of administration and less frequent dosing.

There are presently no pharmaceutical therapeutics approved for the treatment of diabetic retinopathy. There are also no standard and effective therapies for most AMD patients. Given the high unmet medical need for such diseases the market potential for effective medicines is estimated to be several billion dollars.

Patent applications have been lodged covering all disease indications for GHr antisense.

#### Outlook

Following the success of the animal efficacy studies and in light of the significant commercial potential of the compound, the company has decided to move this project, named ATL1103, into development. Orders for bulk quantities of the active pharmaceutical ingredient, to be formulated into injectable product for use in the preclinical safety studies, are expected to be placed with our collaboration partner Isis Pharmaceuticals, Inc, within the first half of 2004.

This result from our drug research pipeline confirms Antisense Therapeutics' ability to use the most advanced second generation antisense technology to quickly and inexpensively generate and test new antisense compounds for clinically validated targets in important human diseases.

#### About Acromegaly

Acromegaly is a serious chronic life shortening disease triggered by excess secretion of growth hormone (GH) by benign pituitary tumours. Oversupply of GH overstimulates liver, fat and kidney cells, through their GH receptors, to produce excess levels of Insulin-Like Growth Factor-I (IGF-I) in the blood manifesting in abnormal growth of the face, hands and feet, and enlargement of body organs including liver, kidney and heart. The primary treatments for acromegaly are to surgically remove the pituitary gland and/or drug therapy to normalize GH and serum IGF- I levels. In North America, Europe and Japan there are approximately 40,000 diagnosed acromegaly patients with about half requiring drug therapy. Drug treatment costs vary depending on dosage and frequency of administration ranging from A\$14,000-\$33,000 per patient per year

#### About Diabetic Retinopathy and Age Related Macular Degeneration (AMD)

Diabetic retinopathy and wet age-related macular degeneration (AMD) are two of the leading causes of vision loss. Over 5 million Americans aged 18 and older are affected by diabetic retinopathy. Around 12,000-24,000 patients with diabetic retinopathy lose their eyesight

each year in the US alone. These conditions are caused by new blood vessel formation in the retina or macula (the central part of the retina). In diabetes, high blood glucose can cause oxygen deprivation, which can stimulate factors that induce additional blood vessels in the retina. In AMD similar factors are thought to stimulate blood vessel production in the macula. These new blood vessels may break and bleed into the eye leading to scarring within the eye. Whilst there are drugs to control diabetes, patients with Type I diabetes who have had their disease for more than 10 years have a 90% chance of developing retinopathy, and about 20% of patients with Type II diabetes will get the disease. Surgical ablative treatments such as photocoagulation (laser therapy) are available but are not completely effective, may cause partial vision loss, and can only be used a limited number of times.

#### About Antisense Therapeutics Limited

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Contact Information: Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999

RECEIVED

2000 NOV 16 P 12: 21

CEFICE OF INTERNATION CORPORATE FINANCE

CIRCADIAN TECHNOLOGIES LIMITED

ABN 32 006 340 567

10 Wallace Avenue, Toorak Victoria 3142 Australia

P.O. Box 23, Toorak, Victoria 3142 Australia

Telephone: +61 3 9826 0399 Fax: +61 3 9824 0083

4 March 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

No of Pages: 2

Dear Sir/Madam

### Re: Purchase of Options in Antisense Therapeutics Limited

We would like to advise that Circadian Technologies Limited has purchased a parcel of 3,405,000 options in Antisense Therapeutics Limited on the market. These options expire on 1 February 2007 and are exercisable at 20 cents each. Circadian now holds, through direct and indirect interests, a total of 95,497,227 full paid ordinary shares (26.9% interest) and 19,725,480 options in Antisense Therapeutics.

Antisense Therapeutics' largest shareholders are Circadian Technologies Limited (26.9%), Isis Pharmaceuticals Inc (11.3%) and Queensland Investment Corporation (4.5%).

Yours faithfully Circadian Technologies Limited

Natalie Korchev Company Secretary

#### About Circadian Technologies Limited

Circadian Technologies Limited (ASX: CIR) was listed on the Australian Stock Exchange in 1985 and provides management and funding for the development and commercialisation of Australian biomedical research.

It aims to identify high potential scientific research projects from within Australian universities and research institutes, focussing on opportunities that have the potential to address large markets or significant unmet medical needs. Circadian is able to provide funds for further project development, in addition to providing the management expertise that is essential if the project is to meet its goal of commercialisation.

Circadian has shareholdings in Optiscan Imaging Limited, Metabolic Pharmaceuticals Limited, Antisense Therapeutics Limited and U.S. based Axon Instruments Inc, companies in which Circadian has been involved in providing management, funding and/or assistance in their listing. Circadian is also the largest shareholder in Amrad Corporation Limited, an Australian pharmaceutical research company.

In addition to retaining shareholdings in these companies, Circadian maintains an active research and development program. Its core neurosciences research projects aim to develop a new treatment specifically for Alzheimer's disease, to develop novel compounds for the treatment of a range of neurodegenerative disorders such as stroke and Parkinson's disease, to develop a family of new analgesics and to develop compounds with potential for enhancing memory. Other projects include the development of a diagnostic for cancers of unknown tissue origin, a novel technology for identification of cancer markers, a new environmentally friendly process for manufacture of a key pharmaceutical raw material (ephedrine) and an extensive patent portfolio in an emerging technology in gene testing (known as in situ hybridisation).

lodging party or agent name	
office, level, building name or PO Box no	
street number & name	
suburb/city	etate/territany wenestende e.e.
telephone	
facsimile	ASS. REQ-A
DX number	
	CONTORALLE
	Australian Securities & Investments Commission form 909
	Notification of Corporations Act 2001
	office at which register is kept 100(1)(d), 172, 271, 1302(4)
	601CZC
company name	ANTISENSE THERAPEUTICS LIMITED
ACN	095 060 745
Details of Register	
•	Register of members
	Register of options
	Register of charges
	Register of holders of debentures
•	Register of debenture holders for non-companies
Details of change	
<b>3</b> .5	change from registered office date of change (d/m/y) / /
	change from principal place of business date of change (d/m/y) / /
	change from other address date of change (d/m/y) 22/ 03 / 2004
Details of other address where change at the office of	
	COMP GILLOTARE HAVESTON SCHOOLS FIT EMAILED
office, level, building name	The Park The
street number & name	503 BOURNE STREET
suburb/city	MELBOURNE state/territory VtC postcode 3000
New address	<b>i</b> r.
New audress	
at the office of	COMPUTERSHARE INVESTOR SERVICES PTY LIMITED
office, level, building name	YARRA FALLS
street number & name	452 JOHNSTON STREET
suburb/city	ABBOTSFORD state/territory VIC postcode 3067
	Does the company occupy these premises?
If NO, name of occupier	COMPUTERSHARE INVESTOR SERVICES PTY LIMITED
•	
occupier's consent	(Tick box to assent to statement required by subsection 100(1)(d)
	\$ 0
	The occupier of the premises has consented in writing to the use of the new address as the place for keeping of the register and has not
	withdrawn that consent.
Signature	
oigilature .	
print name	Mark Diamond capacity Managing Director
sign here	(h) (date 10,03,2004
•	
	Small Business (less than 20 employees), please provide an estimate of the time taken to complete this form
•	Include
	The time actually spent reading the instructions, working on the question and obtaining the information
,	The time spent by all employees in collecting and providing this information
•	
	hrs mins

ASIC registered agent number



12 March 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Antisense Therapeutics Limited: Investor Update - March 2004

Please find attached Antisense Therapeutics Limited's Investor Update.

Yours sincerely

Mark Diamond

Managing Director



March 2004

Dear Shareholder

Welcome to another update on the progress of Antisense Therapeutics' key development projects.

We are pleased to provide this update summarising several recent positive developments.

In summary, our lead projects continue to maintain momentum and are progressing to plan, while I am also very excited about our recent decision to move forward with a new compound.

We appreciate your continued support, and I look forward to bringing you further good news in the future.

Regards

Mark Diamond Chief Executive Officer

### 1. Recent Highlights

- ATL1102 for MS Phase I human clinical trials commenced in August 2003 and have progressed rapidly with both single and multiple dosing schedules now complete. There are favourable preliminary indications from the data that have been collected and analysed.
- ATL1101 for Psoriasis The manufacture of the active pharmaceutical ingredient for the Psoriasis 'proof-of-concept' study is now complete. The precursory animal toxicology studies are scheduled to commence in mid-2004 following successful formulation.
- ATL1103 for Growth Hormone disorders The Company announced that it is developing a
  new compound designed to block Growth Hormone receptor (GHr) expression. Successful
  testing undertaken in mice indicates it has potential as a treatment for growth and sight
  disorders.
- The early filing with the US Food and Drug Administration (FDA) by US biotech company BioGen Idec and its partner Elan of a marketing application for their MS antibody drug Antegren<sup>™</sup> provides Antisense Therapeutics with greater confidence in the likely success of ATL1102. Both Antegren and ATL1102 target the VLA-4 protein, which is considered to be involved in the progression of MS.
- The company released its half-yearly financial results for the six-month period to 31 December 2003, reporting a loss of \$1,626,940 (2002: \$3,882,283). Cash reserves currently stand at \$15 million following successful capital raisings during the period.

#### 2. Project Review

#### ATL1102 for Multiple Sclerosis

ATL1102 is designed to block the synthesis of an immune system component or protein called VLA-4 that is known to play a part in both the onset and progression of multiple sclerosis ('MS').

In August 2003, Antisense Therapeutics commenced Phase I human clinical trials of ATL1102 at the Charterhouse Clinical Research Unit in London.

The aims of these Phase I trials are to obtain information on the pharmacokinetic<sup>1</sup> behaviour of ATL1102 in humans and to assess the safety and tolerability of increasing dose levels of ATL1102 injected as single and multiple doses. Fifty-four healthy volunteers have participated in the placebo-controlled, randomised, double-blind study.

The study has progressed rapidly, having completed both single and multiple dosing schedules.

Laboratory investigations of the biological samples collected during the trial are currently taking place.

Some preliminary data from these clinical trials were presented at the Australian Neuroscience Society Scientific Conference in Melbourne on 30 January 2004. As reported by the Company at this time, preliminary indications from the data collected and analysed so far are favourable in terms of both safety and pharmacokinetics.

Full and final results are expected to be reported mid year.

At present, study designs for the Phase IIa clinical trial are being discussed with potential clinical trialists and contract organisations.

Once final reports are received for the Phase I trial and the results are assessed as satisfactory, the Company will make an application for the Phase IIa patient trial.

Regulatory agency approval and commencement of the Phase IIa trial are targeted for the second half of 2004.

#### **ATL1101 for Psoriasis**

ATL1101 is designed to block the synthesis of the IGF-1 receptor, a protein involved in the regulation of cell growth in psoriasis. The psoriasis project is supported by a Commonwealth Government R&D Start grant of AUD1.1 million.

In July 2003, the company announced its plans to undertake a 'proof of concept' study, which will accelerate the testing of ATL1101 in humans suffering from psoriasis. In this study - also referred to as the small plaque assay (SPA) - a relatively small quantity of ATL1101 will be applied to areas of psoriatic skin on a limited number of patients. The SPA is designed to carefully monitor and also restrict the extent of patients' exposure to the test compound.

This human study is to commence once supplies of drug product are manufactured and the required precursory animal toxicology program is performed. The manufacture of the active

<sup>&</sup>lt;sup>1</sup> "Pharmacokinetics" is how the drug distributes in the body over time after administration, helpful in deciding dosing frequency in future studies.

pharmaceutical ingredient and the analytical work has been completed and the formulation of injectable and cream presentations of ATL1101 is currently underway.

Looking forward, the animal toxicology studies for ATL1101 are scheduled to commence in mid-2004, following completion of the formulation activities. Subject to receiving the relevant approvals to conduct the study, the human 'proof of concept' study is expected to begin in the second half of 2004.

#### ATL1103 for Growth and Sight disorders

Following successful animal testing, Antisense Therapeutics is moving forward on a new compound codenamed ATL1103. ATL1103 is an antisense inhibitor designed to block Growth Hormone receptor (GHr) expression.

The results from animal testing confirm its potential as a treatment for diseases associated with excessive growth hormone action.

These include acromegaly (abnormal growth of organs, face, hands and feet) and two other diseases known to be major causes of blindness - diabetic retinopthy and wet age-related macular degeneration (AMD).

ATL1103 was tested on mice at the University of Queensland by Professor Michael Waters, who is internationally recognised for his research on GHr and associated disorders. The study results are comparable to those achieved by pegvisomant - the latest drug to be approved in Europe and the US for the treatment of acromegaly - in an equivalent animal model.

The animal study results for ATL1103 are being presented by Antisense Therapeutics to an International GH-IGF Symposium in Cairns on 20 April 2004.

ATL1103 may have important clinical advantages over octreotide - which is the most widely used treatment for acromegaly - and pegvisomant, including more convenient route of administration and less frequent dosing.

Sales of the newer drug, pegvisomant, are projected to reach US\$500 million per annum, which indicates both the size of the market and the potential for ATL1103.

There are no pharmaceutical therapeutics approved for the treatment of diabetic retinopathy. There are also no standard and effective therapies for most AMD patients.

The market potential for effective medicines to treat these diseases is estimated at several billion dollars.

Further details regarding ATL1103 and sight and growth disorders is contained in the 24 February 2004 ASX announcement enclosed with this investor update.

#### 3. Market Developments

#### An endorsement for Antisense Therapeutics' MS compound

US Biotech company BioGen Idec and its partner Elan announced that they are planning to file their Multiple Sclerosis drug, Antegren<sup>TM</sup>, with the US Food and Drug Administration (FDA).

This announcement follows the completion by Biogen/Elan of the first year of their two-year Phase III studies of Antegren<sup>™</sup> in MS patients. Whilst the results have not been released, early

discussions with the FDA have been interpreted by commentators as a positive indication of the likelihood of success of the drug in the clinic.

Both BioGen Idec (market cap: US\$19 billion) and Elan (market cap: €5 billion) have enjoyed significant increases in their respective share prices on the release of their news (Biogen's share price has increased by 33 per cent and Elan's by 89 per cent to 4 March 2004).

So, how does this impact on Antisense Therapeutics and, more particularly, the development of its own MS drug, ATL1102?

Both Antegren<sup>TM</sup> and Antisense Therapeutics' MS compound ATL1102 block the VLA-4 protein, which is considered to be responsible for the progression of MS (refer 17 June 2002 Investor Update 'The Rationale for VLA-4 as a Target Treatment for MS' which can be found at www.antisense.com.au).

ATL1102 is a second generation antisense drug designed to act at an earlier stage of the disease process by preventing excessive amounts of VLA-4 being produced.

With its highly specific mechanism of action and well tolerated drug chemistry, ATL1102 may potentially provide important advantages over Antegren<sup>™</sup> in the cost of therapy and method of delivery, as well as improved effectiveness.

The recent Antegren<sup>™</sup> news provides Antisense Therapeutics with greater confidence in the likely success of ATL1102. Also, the submission of the Antegren<sup>™</sup> application to the FDA will establish a path to regulatory approval for ATL1102 and commercially and scientifically validate the Company's MS drug development strategy.

#### 4. Financial Information

Antisense Therapeutics recently announced its financial results for the six-month period to 31 December 2003.

For the half-year, Antisense recorded a loss of \$1,626,940 (2002: \$3,882,283), which included an income tax benefit of \$371,820 (2002: \$nil) and the expensing of all research and development costs incurred.

There were a number of major reasons why the loss was less than what was recorded in the same period in 2002. Among them was the receipt of an R&D Start Grant for the ATL1101 psoriasis project (\$638,700) and a cash rebate received in relation to the Research and Development Tax Concession (\$371,820).

The Company also had less research and development costs this half-year, with the majority of the costs of the manufacturing, development and formulation of ATL1102 having been incurred in 2002.

Also during this six-month period to 31 December 2003, the company raised \$10.4 million through the issue of new shares. Of this amount, \$5 million was raised through a private placement to Australian institutions and professional investors and a further \$5.4 million was raised pursuant to the company's Share Purchase Plan.

Cash Reserves now stand at \$15 million.

Computershare RECEIVED

Tuesday 16 March 2004

Company Announcements

Fax - 1900 999 279 - 5 Pages

Attention: Ms Pam Ross

2004 NOV 16 P 12: 21

Investor Services

Australian Stock Exchange Limited

FIOF OF INTERMATIONAL Computershare Investor Services Pty Limited
GORPORATE FINANCE
ABN 48076279277

Level Twelve 565 Bourke St Melbourne Victoria 3000 Australia GPO Box 2975EE Melbourne Victoria 3001 Australia

> DX Box 30941 Australia Investor Enquiries 1300 850 505 Canada Telephone 61 3 9611 5711 Channel Islands Facsimile 61 3 9611 5710 Germany

www.computershare.com Hong Kong reland New Zealand South Africa United Kingdom

USA

Change Of Address Notification

Dear Ms Ross,

With effect from commencement of business on 22 March 2004, the Melbourne Office of Computershare Investor Services Pty Limited (CIS) is moving:

From

Level 12, 565 Bourke Street, Melbourne Victoria 3000

Yarra Falls, 452 Johnston Street, Abbotsford, Victoria 3067 Main Switchboard - 03 9415 5000 Enquiries outside Australia - +61 3 9415 4000 Facsimile - +61 3 9473 2500

The postal address remains unchanged: GPO Box 2975, Melbourne, Victoria 3001

Our 1300 and 1800 prefixed numbers also remain unchanged.

Lodgement of documentation by member organisations, security holders, and other interested parties must be made to the new address with effect from 22 March 2004.

Attached is a list of the clients of CIS Melbourne Office who are affected by this move. Could you please arrange for the details concerning the location of the securities registers to be amended.

Should you have any further questions relating to this matter, please contact the undersigned.

Yours Sincerely,

Peter Vaughan

Computershare Investor Services Pty Limited

# **Computershare**

Ken are consensed	N. W. W. C.
	Constitution of the consti
AAT	Autron Corporation Limited
ADA	Adacel Technologies Limited
ADL	Admerex Limited
ADT	Advent Limited
AEO	Austereo Group Limited
AET	Ausmeit Limited
AFL	Australian Pure Fruits Limited
AGS	Alliance Resources Limited
AIX	Australian Infrastructure Fund
ALH	Australian Leisure & Hospitality Group Limited
AMC	Amcor Limited
AML	AMRAD Corporation Limited
AMZ	Amoor Investments (New Zealand) Limited
ANN	Ansell Limited
ANP	Antisense Therapeutics Limited
ANX	Anadis Limited
ANZ	Australia and New Zealand Banking Group Limited
ARP	ARB Corporation Limited
A\$K	Amskan Limited
ASU	Alpha Technologies Corporation Limited
ATG	Austin Group Limited
ATH	A Tech Holdings Limited
AUI	Australian United Investment Company Limited
AVC	Australian Visual Communications Limited
AVF	Australian Value Funds Management Limited
AVJ	A V Jennings Homes Limited
AWB	AWB Limited
AWC	Alumina Limited
AXA	AXA Asia Pacific Holdings Limited
AXH	Adex Holdings Limited
AXN	Axon Instruments Inc.
BOC	Bougainville Copper Limited
BAX	Baxter Group Limited
BDG	Bendigo Mining NL
BDM	Biodiem Limited
BER	Berklee Limited
BFL	Bonlac Foods Limited
BGF	Ballarat Goldfields NL
BHP	BHP Billiton Limited
BKA	Buka Minerals Limited
BKV	Big Kev's Limited
BOL	Boom Logistics Limited
BSN	Bisan Limited
CAL	Citic Australia Trading Limited
CBC	China Convergent Corporation Limited
CBD	CBD Energy Limited
CDC	Child Care Centres Australia Limited
CDL	Canada Land Ltd
CDX	CDS Technologies Limited
CEQ	Central Equity Limited
CGO	CPT Global Limited
CID	Citadel Pooled Development Limited
CIH	China Construction Holdings Limited
ÇIR	Circadian Technologies Limited
CLL	P. Cleland Enterprises Limited

# **Computershare**

	•
CML	Coles Myer Limited
CPI	CPI Group Limited
CRO	Crown Limited
CRP	Cryptome Pharmaceutical Limited
ÇSL	CSL Limited
CST	Cellestis Limited
CUE	Cue Energy Resources Limited
CTY	Country Road Limited
DFT	Datafast Telecommunications Limited
DMY	Dromana Estates Limited
DNI	Digital Now Inc
DPL	Daily Planet Limited, The
DUI	Diversified United Investment Limited
EAC	East African Coffee Plantations Limited
EIF	Eiffel Technologies Limited
EMI	emitch Limited
EPR	Essential Petroleum Resources Limited
EPT	Epitan Limited
EQT	Equity Trustees Limited
ERH	Eromanga Hydrocarbons NL
EWL	Entertainment World Limited
EWN	Erawan Company Limited
FEA	Forest Enterprises Australia Limited
FGL	Foster's Group Limited
FRM	Farm Pride Foods Limited
FUN	Funtastic Limited
gan gap	CFS Gandel Retail Trust Gale Pacific Limited
GAS	Gasnet Australia Group
GCN	GoConnect Limited
GHG	Grand Hotel Group Limited
GNS	Gunns Limited
GUD	GUD Holdings Limited
HLT	Healthpoint Technologies Limited
HWI	Housewares International Limited
IAS	IASBet Limited
IAT	latia Limited
ICP	International Concert Attractions Limited
IGP	Investor Group Limited
INO	Innovonics Limited
INT	Intermoco Limited
ION	ION Limited
IRN	Indophil Resources NL
ITE	I T & E Limited
<b>IWL</b>	IWL Limited
IXL	IXLA Limited
JBH	JB Hi-Fi Limited
JRV	Jervois Mining Limited
KNH	Koon Holdings Ltd
LVO	Lakas Oil MI

LKO

LKP

LMC

L\$G

MBF

MBP

MCH

Lakes Oil NL

Lako Pacific Limited

Lemame Corporation Limited

Lion Selection Group Limited

Murchison Holdings Limited

Metabolic Pharmaceuticals Limited

MBF Carpenters Limited



MCL	M2M Corporation Limited
MCP	McPherson's Limited
MDL	Mineral Deposits Limited
MMS	McMillan Shakespeare Limited
1.101.4	MDI Mines Limited

MPM MPI Mines Limited
MRY Monteray Group Limited
MSI Multistack International Limited

MUL Multiemedia Limited

MVP Medical Developments International Limited MWC Media World Communications Limited

MYO MYOB Limited

NAL Norwood Abbey Limited
NCI National Can Industries Limited
NFO Network Foods Limited
NHM New Holland Mining Limited

NLX Nylex Limited

NNZ Nylex (New Zealand) Limited NPH New Privateer Holdings Limited

NUF Nufarm Limited NWK Network Limited

OCO Oriel Communications Limited
OIL Optiscan Imaging Limited

OKN Oakton Limited
PAS Pasminco Limited

PBT Prana Biotechnology Limited
PCE Pinnacle VRB Limited
PCO Pracom Limited

PHL Pearl Healthcare Limited
PMV Premier Investments Limited
POH Phosphagenics Limited

PPX PaperlinX Limited

PRG Programmed Maintenance Services Limited

PRM Plenty River Corporation Limited
PRV Premium Investors Limited
PSG Palm Springs Limited
QST Quest Investments Limited

RBS Roberts Limited

RCL Repco Corporation Limited
RDF Redflex Holdings Limited
REH Reece Australia Limited
RIO Rio Tinto Limited
RMG RMG Limited

RNG Range River Gold Ltd.

SCE Suntech Environmental Group Limited

SED Sedimentary Holdings Limited
SEE Sun Capital Group Limited
SEN Senetas Corporation Limited
SHV Select Harvests Limited
SIG Sigma Company Limited
SKE Skilled Engineering Limited
SKS Stokes (Australasia) Limited

SMX SMS Management & Technology Limited

SNO Snowball Group Limited SPC SPC Ardmona Limited

SPD Strategic Pooled Development Limited
SPL Starpharma Pooled Development Limited

# **Computershare**

SPT	Spotless Group Limited
SSI	Sino Securities International Ltd
STP	SteriCorp Limited
STS	Structural Systems Limited
SWG	Swish Group Limited, The
TAW	Tawana Resources NL
TÇL	Transurban Group
TCS	Transurban CARS Trust
TGG	Templeton Global Growth Fund Ltd
TGR	Tassal Group Limited
TIM	Timbercorp Limited
TKG	Takoradi Limited
TOD	Timbercorp Orchard Trust
TOL	Toll Holdings Limited
TOR	Ticor Limited
TPX	Tasmanian Perpetual Trustees Limited
TRG	Treasury Group Limited
TRU	Trust Company of Australia Limited
TRY	Troy Resources NL
TSS	Tassal Limited
TTI	Traffic Technologies Ltd
TXT	Text Media Limited
TZL	TZ Limited
UEC	UECOMM Limited
USH	US Masters Holdings Limited
UXC	UXC Limited
VHL	Virax Holdings Limited
VIA	Viagold Capital Limited
VRL	Village Roadshow Limited
WBA	Webster Limited
WFL	Willmott Forests Limited
W)F	Wine Investment Fund Limited
WWA .	Wridgways Australia Limited
WWH	Water Wheel Holdings Limited
XQA	Queensland Electricity Board
XQB	Brisbane City Council
XQL	Queensland Treasury Corporation
XSQ	South Australian Government Financing Authority
XTA	Hydro Electricity Commission of Tasmania
XVG	Treasury Corporation of Victoria
XWD	Western Australian Treasury Corporation

AuSelect Limited
Contango Microcap Limited
Mount Rommel Mining Limited
Pacific Brands Limited

CONTRACTOR OF SERVICE AND ADDRESS OF THE PARTY OF THE PAR

Zeolite Australia Limited

Warrenmang Limited

Zinifex Limited

ZEL

16 March 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Updated Corporate Presentation

Please find attached Antisense Therapeutics Limited's updated company presentation.

The attached presentation has been updated to include the company's latest development project, ATL1103 for Growth and Sight Disorders.

Yours sincerely

Mark Diamond
Managing Director



# Antisense Therapeutics Limited

(ASX : ANP)

March 2004

# Antisense Therapeutics Ltd

- ♦ Listed on ASX Dec 2001
- ♦ Total funds raised to date: A\$28.5 M
- ♦ Market Cap: A\$51.5 M
- ♦ Key Shareholders
  - Circadian 20%
  - Syngene 15% (42% Circadian)
  - Isis 11%
  - QIC 5%
- ♦ Cash reserves of A\$15 M, no borrowings



### **Board of Directors**

- ♦ Bob Moses, Chairman (ex VP of CSL)
- ♦ Mark Diamond, CEO (ex Faulding)
- ♦ Dr Chris Belyea (CEO Metabolic)
- ◆ Dr Stanley Crooke (Founder ISIS Pharmaceuticals, Inc)
- ◆ Prof Graham Mitchell (Foursight/CSL)
- ◆ Prof George Werther (MCRI)

### ANP's Mission

- ♦ Create, develop and commercialize novel antisense pharmaceuticals for large and/or niche unmet markets
- ◆ Select targets where our technology will provide clear competitive advantages

### Business strategy

- ◆ Leverage 14 years of Isis antisense technology development
- ◆ Fast track existing lead projects through pre-clinical and clinical development
- ♦ Create pipeline of new antisense therapeutics
- ♦ Commercialise those that are successful in clinical testing via licensing/partnering

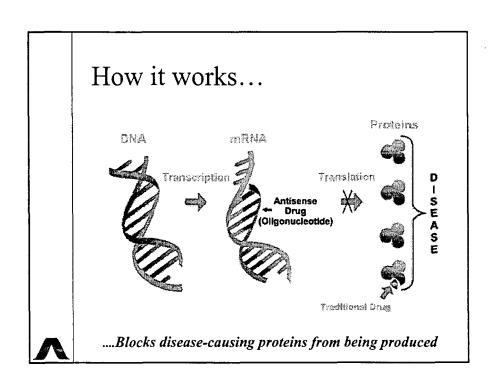


- ♦ Acknowledged global leader in antisense
- ♦ Over US \$1B invested in antisense chemistries
- ♦ More than 1,000 patents issued
- ♦ 1 FDA drug approved, 8 in late stage clinical development
- ♦ Deals with large market cap companies (eg Lilly and Amgen)



# What is antisense technology?

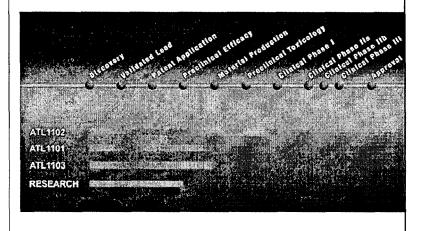
- A fundamentally different approach to making medicine:
- ♦ Unprecedented target specificity and selectivity
- ♦ Most current drugs interfere with the activity of proteins that cause disease
- ♦ Antisense drugs go to work earlier, they block the manufacture of the target protein



# Technical advantages

- ◆ Mature technology (20 years in development)
- ◆ Drug discovery and research is faster and more predictable
- ◆ Compounds are potentially more selective, effective and less toxic
- ♦ Broad disease application
- ♦ Dosing advantages (route and frequency)

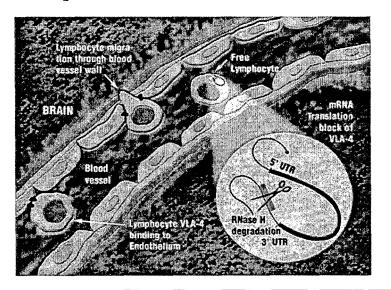
# Development Pipeline



- ♦ MS is a progressive neurological disease
- ♦ Onset of MS is usually at young age (20 -40 years)
- ♦ MS affects 2.5 million people world-wide
- ◆ No cure; drugs aim to delay disease progression
- ♦ Beta-interferon (1a, 1b) leading therapy
  - Biogen, Serono, Schering AG
- ◆ Need for more effective drugs with less side effects
- ♦ Global drug sales for MS >US\$ 2.5 billion in 2003



## Multiple sclerosis - ATL1102





- ♦ Product
  - Antisense inhibitor to VLA-4 protein which contributes to onset of disease
  - Confirmed activity in pre-clinical mouse model of MS (also other inflammatory disorders asthma & arthritis)



# Multiple Sclerosis - ATL1102

- ♦ Product (cont)
  - Biogen Idec's Antegren<sup>TM</sup> (also targets VLA-4) in Phase III trials
    - Filing marketing application with FDA based on interim 1 year phase III data
    - Provides greater confidence in likelihood of clinical success of ATL1102
    - Anticipate efficacy, dosing and cost advantages with ATL1102



# Problems with Current Therapies\*

# Antegren\* • Different

In development

# ATL1102

- Partial or no response to βIFNs & Copaxone
- Different mechanism of action
- Different mechanism/no neutralising antibodies

- ♦ Flu-like symptoms
- No flu-like symptoms
- No flu-like symptoms

- Dosing too frequent
- ♦ Only 1x/month
- ◆ Dosing TBC potentially 1x/week

or 1x/month

- Don't want injection responsibility/ inconvenience
- IV done by doctor
- Sub-cutaneous, potential needless injection/oral



\* Source: Biogen website – The JP Morgan 21<sup>st</sup> Annual Healthcare Conference Presentation (14/1/03)

# Multiple Sclerosis - ATL1102

- ♦ Progress
  - Manufactured drug product for Phase I and IIa studies
  - Phase I human trial underway dosing completed
  - Preliminary results presented at Australian Neurosciences Conference in January '04



- ♦ Outlook
  - Phase I trial final reports due mid '04
  - Following successful completion of
     Phase I trial company will make an
     application for the Phase IIa patient trial
  - Phase IIa trials scheduled to commence in 2<sup>nd</sup> half 2004



### Psoriasis Treatment - ATL1101

- ♦ Disease & Market
  - Chronic non-contagious skin disorder
  - Affects 1-2% of population
  - Global drug sales forecast to exceed
     US\$2 billion by 2007 (Frost & Sullivan)
  - Need for more effective therapies
- ♦ Product
  - Antisense inhibitor to IGF-IR regulates cell growth
  - Developing topical formulation

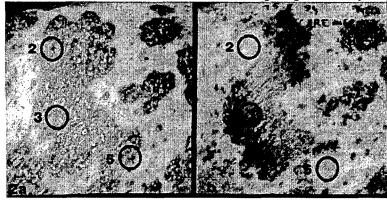


# Psoriasis Treatment - ATL1101

- **♦** Progress
  - Completed pre-clinical efficacy program
  - Awarded A\$1.1 million government grant
  - "Proof of Concept" (PoC) study in psoriasis patients
    - Manufacture of compound for study underway
    - Contracted commercial laboratory to conduct animal toxicology program

# Human proof of concept strategy:

Psoriasis small plaque assay



Rappersberger et al., Clearing of psoriasis by a novel immunosuppressive macrolide. *J Invest Dermatol* **106**, 701-10 (1996).

### Psoriasis Treatment - ATL1101

- ♦ Outlook
  - Commence PoC trial in 2<sup>nd</sup> half 2004 after toxicology studies successfully completed and relevant approvals received



# Research Pipeline

- ◆ Projects that target diseases of growth, vision and major inflammatory diseases
- ♦ Animal studies are at various stages of completion
- ♦ Most advanced research pipeline project: ATL1103 for growth & sight disorders
  - Project to move into development



# ATL1103 for growth & sight disorders

### Growth - Acromegaly

- ♦ The Disease
  - A disorder of excess growth hormone in adults associated with excess serum IGF-1
  - Affects 40,000\* people
- ♦ The Market
  - High treatment costs (from A\$14K-\$33K/annum)
  - Somatostatin analogue effective in ~ 60% of patients
  - Trovert<sup>TM</sup> sales projected to reach US\$500 million



\* US, Europe and Japan

# ATL1103 for growth & sight disorders <u>Sight - Diabetic Retinopathy</u>

- ♦ The Disease
  - Neovascularisation of the retina leading to blindness
  - High prevalence: over 5 million Americans affected by diabetic retinopathy
  - 12,000-24,000 new cases of blindness per year in US
- ♦ The Market
  - No approved drug treatments for diabetic retinopathy



- \$Billion market potential

### ATL1103 for growth & sight disorders

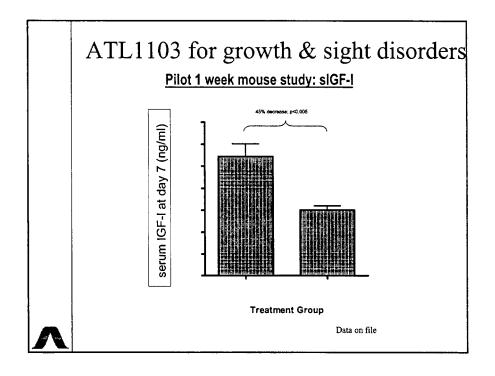
- ♦ Product
  - Antisense inhibitor to the GH receptor
  - GH action is mediated through IGF-1 hormone
  - Acromegalics have elevated levels of both GH and IGF-1
  - Acromegaly treatment involves normalising IGF-I levels
  - Reduction of IGF-I levels is associated with clinical improvement in retinopathy



### ATL1103 for growth & sight disorders

- ♦ Results of Animal Studies
  - IGF-1 suppression by ATL1103 comparable to Trovert<sup>TM</sup> (existing treatment for acromegaly) in an equivalent mouse model
  - Data to be presented at 2nd International Symposium on GH & IGF-I, Cairns, Australia, April 2004
  - Patent applications filed





# ATL1103 for growth & sight disorders

### Why ATL1103?

- ♦ Consistent with and validates ATL business plan
  - Grow business and diversify risk through product pipeline development
- ♦ Attractive Project
  - Significant market potential
  - GHr target is clinically validated
  - Ability to test for clinical endpoint (serum IGF-I) in early human studies
  - Limited competition
  - Potential dosing, administration and cost advantages

# ATL1103 for growth & sight disorders Competitor drugs in acromegaly

Drug	Efficacy	Route	Dosing Frequency	Cost (A\$)
GHr antagonist Trovert <sup>TM</sup>	90-95%	sc	1 x per day	\$20-25,000/yr estimated
Somatostatin analogues (octreotide) Sandostatin <sup>TM</sup> Sandostatin LAR <sup>TM</sup>	65% 65%	sc im depot	3 x per day 1 x per month	\$14 -33,000/yr*
Dopamine agonists Parlodel <sup>TM</sup> Dostinex <sup>TM</sup>	10% >10%	oral oral	4 x per day 2 x per week	



\*Annual treatment costs vary depending on dosage and frequency from A\$14-33000 per patient/year

# ATL1103 for growth & sight disorders

### Outlook

◆ Place order for bulk drug product to commence preclinical safety studies



#### Outlook Project Value Driver Timing ATL1102 ◆Complete Phase I 1st half '04 MS 2<sup>nd</sup> half '04 ♦ Start Phase IIa ◆ Partnering objective Concl Ph IIa 1st half '04 ATL1101 ◆ Complete product manufacture Psoriasis and toxicology program ◆ Start "Proof of Concept" study 2<sup>nd</sup> half '04 ◆ Partnering objective Concl "PoC" ATL1103 1st half'04 ♦ Commence product manufacture for pre-clinical Acromegaly toxicology

### ANP – Investment Fundamentals

- ◆ Attractive product pipeline
  - Validated targets (lower development risk)
  - Products with platform based competitive advantages
  - Significant market potential
- ◆ Track record for hitting development milestones
  - Mature, efficient, and predictable platform technology
  - High quality and effective collaborations (Isis/MCRI)
  - Experienced management team
- ♦ Clear commercialisation objectives
- ♦ Near term key value drivers
  - ATL1102 & ATL1101 in patient trials in '04



MAININ IL DISS



Rule 2.7, 3.10.3, 3.10.4, 3.10.5

# Appendix 3B

# New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002.

Antı	Antisense Therapeutics Limited				
ABN					
41 0	95 060 745				
We (	We (the entity) give ASX the following information.				
	rt 1 - All issues nust complete the relevant sections (attach sh	neets if there is not enough space).			
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	Ordinary Shares			
2	Number of *securities issued or to be issued (if known) or maximum number which may be issued	400			
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	Exercise of 400 ANPO options at \$0.20 each.			

Name of entity

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	Yes	
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
5	Issue price or consideration	\$0.20 cents	
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	Exercise of 400 ANPO	O options
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	15 March 2004	
		L	
		Number	+Class
8	Number and *class of all *securities quoted on ASX (including the securities in clause 2 if applicable)	355,253,750 91,467,365	Ordinary Shares (ANP) Options (ANPO)

<sup>+</sup> See chapter 19 for defined terms.

9 Number and \*class of all \*securities not quoted on ASX (including the securities in clause 2 if applicable)

Number	+Class
11,500,000	Restricted options expiring 31 July 2005 exercisable at 20 cents (ANPAM)
20,000,000	Restricted options expiring 30 November 2006 exercisable at 20 cents (ANPAO)
2,450,000	Options expiring 31 July 2005 exercisable at 20 cents (ANPAQ)

Dividend policy (in the case of a trust, distribution policy) on the increased capital (interests)

N/A		

### Part 2 - Bonus issue or pro rata issue

11	Is security holder approval required?	N/A
	,	
12	Is the issue renounceable or non-renounceable?	N/A
13	Ratio in which the *securities will be offered	N/A
14	<sup>+</sup> Class of <sup>+</sup> securities to which the offer relates	N/A
15	*Record date to determine entitlements	N/A
16	Will holdings on different registers (or subregisters) be aggregated for calculating entitlements?	N/A
17	Policy for deciding entitlements in relation to fractions	N/A
18	Names of countries in which the entity has *security holders who will not be sent new issue documents	N/A
	Note: Security holders must be told how their entitlements are to be dealt with.	
	Cross reference: rule 7.7.	

11/3/2002 Appendix 3B Page 3

<sup>+</sup> See chapter 19 for defined terms.

	_	
19	Closing date for receipt of acceptances or renunciations	N/A
20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a broker and accept for the balance?	N/A

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

32	How do *security holders dispose of their entitlements (except by sale through a broker)?	N/A
33	<sup>+</sup> Despatch date	N/A
	t 3 - Quotation of secur ed only complete this section if you are app	
34	Type of securities (tick one)	
(a)	Securities described in Part 1	
(b)		d of the escrowed period, partly paid securities that become fully paid, when restriction ends, securities issued on expiry or conversion of
Enti	ties that have ticked box 34(	a)
	tional securities forming a new cla additional securities do not form a new clas	
Tick to docum	o indicate you are providing the informa ents	ntion or
35		y securities, the names of the 20 largest holders of the number and percentage of additional *securities held b
36	+securities setting out the nur 1 - 1,000	ty securities, a distribution schedule of the additionants and the categories
	1,001 - 5,000 5,001 - 10,000 10,001 - 100,000 100,001 and over	
37	A copy of any trust deed for	the additional <sup>+</sup> securities
(now g	go to 43)	

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

Entities that have ticked box 34(b)	<b>Entities</b>	that	have	ticked	box	340	(b)
-------------------------------------	-----------------	------	------	--------	-----	-----	-----

38	Number of securities for which †quotation is sought	N/A	
39	Class of *securities for which quotation is sought	N/A	
40	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	N/A	
	If the additional securities do not rank equally, please state:  • the date from which they do  • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment		
41	Reason for request for quotation now	N/A	<del> </del>
	Example: In the case of restricted securities, end of restriction period		
	(if issued upon conversion of another security, clearly identify that other security)		
		Number	+Closs
	N. 1 141 6114		+Class
42	Number and *class of all *securities quoted on ASX (including the securities in clause 38)	N/A	N/A

(now go to 43)

11/3/2002

<sup>+</sup> See chapter 19 for defined terms.

#### All entities

#### Fees

Payment method (tick one)

Cheque attached

Electronic payment made

Note: Payment may be made electronically if Appendix 3B is given to ASX electronically at the same time.

Periodic payment as agreed with the home branch has been arranged

Note: Arrangements can be made for employee incentive schemes that involve frequent issues of securities.

#### Quotation agreement

- <sup>†</sup>Quotation of our additional \*securities is in ASX's absolute discretion. ASX may quote the \*securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the <sup>+</sup>securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before 'quotation of the 'securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here: Natalie Korchev Date: 8 April 2004

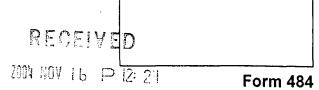
Company secretary

Print name: Natalie Korchev

== == == == ==

11/3/2002 Appendix 3B Page 8

<sup>+</sup> See chapter 19 for defined terms.



Corporations Act 2001 TRICE OF IMPERMATION AL CORPORATE FINANCE

## Change to company details

Sections A. I	B or C ma	v be lodge	ed independent	y with this signed	d cover page to notif	y ASIC of:
---------------	-----------	------------	----------------	--------------------	-----------------------	------------

- A1 Change of address
- A2 Change of name officeholders or members
- A3 Change ultimate holding company
- B1 Cease company officeholder B2 Appoint company officeholder
- B3 Special purpose company

- C1 Cancellation of shares
- C2 Issue of shares
- C3 Change to share structure
- C4 Changes to the register of members

Company details	Company name					
· · · · · · · · · · · · · · · · · · ·	ANTISENSE THERAPEUTICS LIMITED					
Refer to guide for information about	ACN/ABN	Corporate key				
corporate key	41 095 060 745	78841339				
Lodgement details	Who should ASIC contact if there is a query about this form?					
-	Name					
	NATALLE KORCHEV					
	ASIC registered agent number (if applicable)					
	Telephone number					
	(03) 9827 8999					
	Postal address					
·	LEVEL 1, 10 WALLACE AVENUE					
	TOORAK VIC 3142					
	Total number of pages including this cover sheet Please provide an estimate of the time taken to complete this form					
	hrs	mins				
This form must be signed by a current	I certify that the information in this cover sheet and the attached sections Name  NATALIE KORCHEV	of this form are true and complete.				
	Capacity					
	Director					
	Company secretary					
	Signature					
	N. Korchev					
	Date signed					
	[1]3/[a]4/[a]4 p 0) [M M] (Y Y					
Lodgement	[D D] [M M] [Y Y]  Send completed and signed forms to: For he	lp or more information				
Lodgement	[O O] [M M] [O O]					

#### A1 Change of address This section allows a new address to be applied to one or more purposes (ie registered office, principal place of business, company officeholder or member). You must copy and attach another Section A1 for each new address. At the office of, C/- (if applicable) New address A PO Box is only allowed for a member address Office, unit, level, or PO Box number (A PO Box is only allowed for a member address) Street number and Street name て WALLEN ROAD Suburb/City State/Territory VICTORIA HAUTHORN Postcode Country (if not Australia) 3122 Date of change Date of change For members' address changes, use the 0 date of change to the members' register Registered office address Apply address to ou can apply the new address to one or If the registered office has changed, does the company occupy the premises? nore of the following - registered office, \_ J yes principal place of business, etc. по if no, name of occupier? Registered office address A change to the registered office address takes effect either 7 days after lodgement of the notice or a Occupier's consent (Select box to indicate the statement below is correct) later date specified in the notice. The occupier of the premises has consented in writing to the use of the specified address as the address of the registered office of the company and has not withdrawn that consent. Principal place of business address Company officeholder's residential address Given names Family name MARK DIAMOND Date of birth 03,0 Place of birth (town/city) (state/country) MELBOURNE VICTORIA Family name Given names 2 Date of birth (state/country) Place of birth (town/city) Member's address

Member's address If there are more than 20 members in a share class, only address changes for the top 20 need be notified.

Family name	Given names
Family name	Given names
When a member is a company, not a person company name (only if a member)	on

2

ACN/ ARBN/ ABN Country of incorporation (if not Australia)

## C2 Issue of shares

List details of new share issues in the following table.

	Number of shares issu		Amount paid per share		kmount unpaid per shi	are	
ORD		400	20	cents	7	lil	
		<del> </del>			<del></del>		_
diest date of characteristics	earliest date that any of t	he above changes occu	urred				
D] [M N	II Y YI	ere some or all of the sh	nares issued under a Written o	ntract?			
	etary companies must all Form 208 or a copy of th		certifying that all stamp duties	have been paid. Publ	ic companies must als	so lodge a Form 20	7Z
No	(교육) 등 기계						 
if na, proprie	tary companies are not re	equired to provide any f	hudhar daarmaada uulb dhia fa'	m. Public companies	must also lodge a For	rm 208	
Change t	o share struct	<u> </u>	ururer documents with this for	mar danc companies	must also logge a roi		
ere a change to th	o share struct	LUTE as occurred (eg. as a re	esult of the issue or cancellation	n of shares), please s Total number of shares (current	·····································		ISSO
ere a change to the cted. Details of sh Share	O share struct e share structure table hare classes not affected Full title if not standar	LUTE as occurred (eg. as a re	esult of the issue or cancellation	n of shares), please s Total number of shares (current after changes)	Total amount paid on these shares	ails for the share cla Total amount unpaid on these shares	ISS
ere a change to the cted. Details of sh Share class code	o share struct e share structure table ha are classes not affected Full title if not standar	Lure as occurred (eg. as a re by the change are not r	esult of the issue or cancellation equired here.	n of shares), please s Total number of shares (current after changes)	Total amount paid on these shares	Total amount unpaid on these shares	nsse
ere a change to the ched. Details of she share class code	o share struct e share structure table ha are classes not affected Full title if not standar	as occurred (eg. as a reby the change are not reference).	esult of the issue or cancellation equired here.	Total number of shares (current after changes)	Total amount paid on these shares	ails for the share classification to the season of the sea	ussi
ere a change to the ched. Details of she share class code	o share struct e share structure table ha are classes not affected Full title if not standar	as occurred (eg. as a reby the change are not reference).	esult of the issue or cancellation equired here.	Total number of shares (current after changes)	Total amount paid on these shares	ails for the share classification to the season of the sea	nss
ere a change to the cted. Details of she share class code  ORD  OPTIONS  arliest date of chase indicate the DD [M]	o share struct e share structure table hare classes not affected Full title if not standar  ORDINARY  OPTIONS OUT	as occurred (eg. as a reby the change are not referenced)  FULLY PAID  ER ORDINARY	esult of the issue or cancellation equired here.  SHARES  SHARES	Total number of shares (current after changes)	Total amount paid on these shares	ails for the share classification to the season of the sea	nssk
ere a change to the cted. Details of she share class code  ORD  OPTIONS  arliest date of chase indicate the DD [M]	o share structure table have classes not affected Full title if not standard ORDINARY OPTIONS OUR ange earliest date that any of MI MY MI	ture as occurred (eg. as a re by the change are not re rd  FULLY PAID  ER ORDINARY  the above changes occ	esult of the issue or cancellation equired here.  SHARES  SHARES	Total number of shares (current after changes)  125, 417,365	Total amount paid on these shares  35,105,95 .53	ails for the share classification in the season of the shares and the shares are shares	asset .

## C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- · If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to the name indicate the name indicate the name in the member whose thanged	ame and address		y name		siven names			
langeu		OR Comp	any name					· · · · · · · · · · · · · · · · · · ·
		ACN/ARBN	ABN	S. S				
		Office, unit,	level, or PO Box	number				
		Street numb	er and Street na	ime	STATE OF SERVICE			
)		Suburb/City				ng kapanan dalah kebanah dalam Kabanah dalah kebanah dalam Kabanah dalah kebanah dalam	State/	Territory
		Postcode		Country (if no	t Australia)			
arliest date of char lease indicate the e f the following chan	arliest date that a	السالسا	$\square \square_{l} \square$	V)				
The changes are								
Share class code	Shares increased by	Shares decreased by (number)	Total number now held	*Total \$ paid on these shares	*Total \$ unpaid on these	Fully paid (y/n)	Beneficially held (y/n)	Top 20 member (y/n)
	(number)	(namber)			shares		٠	
	(number)	(number)			4.0			
	(number)	(number)			4.0			
	(number)	(number)			4.0			
	(number)	(number)			4.0			
		provide these details	s		4.0			

he changes apply to lease indicate the name and address	Family name	Given names		
the member whose shareholding has nanged	OR			
·	Company name		· · · · · · · · · · · · · · · · · · ·	
	ACN/ARBN/ABN			
	Office, unit, level, or PO Box nu	mber		
	Street number and Street name			
	Suburb/City			214 EV.
			Ctate/Tomites	
	Postcode	Country (if not Australia)		
lease indicate the earliest date that any	Postcode  Date of change			
lease indicate the earliest date that any	Postcode  Date of change	Country (If not Australia) Y)		
ease indicate the earliest date that any the following changes occurred.  The changes are  Share class Shares S code increased by d	Postcode  Date of change  [D D] [M M] [Y  hares  Total number ecreased by now held			
ease indicate the earliest date that any the following changes occurred.  The changes are  Share class Shares S code increased by d	Postcode  Date of change  Do D [M M] [Y]  hares Total number ecreased by now held	*Total \$ paid *Total \$ Fully paid on these unpaid (y/n) shares on these	Beneficially Top 20	
Share class Shares S code increased by d	Postcode  Date of change  Do D [M M] [Y]  hares Total number ecreased by now held	*Total \$ paid *Total \$ Fully paid on these unpaid (y/n) shares on these	Beneficially Top 20	
lease indicate the earliest date that any fithe following changes occurred.  The changes are  Share class Shares S code increased by d	Postcode  Date of change  Do D [M M] [Y]  hares Total number ecreased by now held	*Total \$ paid *Total \$ Fully paid on these unpaid (y/n) shares on these	Beneficially Top 20	

C4 Continued... Further changes to the register of members

Section C Page 5 of 5

register

(New members only)

Date of entry of member's name in

Date of entry

D] [M

M] [Y

D

20 April 2004

#### ATL1103 Animal Study Results to be presented at International Symposium

On 24 February 2004, Antisense Therapeutics announced that based on successful animal studies, it had decided to move a new antisense compound, codenamed ATL1103, into development. ATL1103 is an antisense inhibitor designed to block Growth Hormone receptor (GHr) expression.

The results from animal testing confirm its potential as a treatment for diseases associated with excessive growth hormone action. These include acromegaly (abnormal growth of organs, face, hands and/or feet) and two other diseases known to be major causes of blindness – diabetic retinopathy and wet age-related macular degeneration (AMD).

Today these animal study results for ATL1103 are being presented by Antisense Therapeutics to an International GH-IGF Symposium in Cairns. The abstract document submitted to the Symposium and the presentation slides are attached.

As previously reported, the animal study results for ATL1103 appear to be similar to those achieved by the latest drug approved in Europe and the US for the treatment of acromegaly in an equivalent animal model. ATL1103 may have important clinical advantages over existing therapeutics for acromegaly, including more convenient route of administration and less frequent dosing.

There are no pharmaceutical therapeutics approved for the treatment of diabetic retinopathy. There are also no standard and effective therapies for most AMD patients. The market potential for effective medicines to treat these diseases is estimated at several billion dollars.

#### About Antisense Therapeutics Limited

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS), Queensland Investment Corporation and the Murdoch Childrens Research Institute.

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999

## REDUCTION IN GHR mRNA, GH BINDING AND SERUM IGF-I LEVELS IN MICE TREATED WITH GH RECEPTOR ANTISENSE OLIGONUCLEOTIDE

Tachas G<sup>1\*</sup>, Rao M<sup>2</sup>, Lofthouse S A<sup>1</sup>, Wraight C J<sup>1</sup>, Waters M J<sup>2</sup>

- (1) Antisense Therapeutics Ltd, Vic 3142 Australia;
- (2) University of Queensland, Qld 4072 Australia

Reduction of insulin-like growth factor-I (IGF-I) levels in serum is associated with improved clinical outcomes in acromegaly and diabetic retinopathy patients. This study reports a novel means of achieving such a reduction through the use of antisense oligonucleotide (ASO). ASO targeted to the mouse growth hormone receptor (GHR) was administered to mice every second day in seven or fourteen day studies, at doses from 3mg/kg to 30mg/kg. After seven days of treatment a 45% decrease in serum IGF-I levels was observed in mice treated with 30mg/kg ASO compared to saline control treated mice. A 39% decrease in [125]-bGH specific binding to liver cell membranes collected from ASO treated mice was also observed compared to saline control mice. After 14 days there was an age related overall increase in serum IGF-I levels, however this increase was significantly reduced in mice treated with ASO at 10mg/kg and 20mg/kg compared to oligonucleotide control groups. The reduction in serum IGF-I at 14 days was dependent on dose, with 39-43% decrease in levels achieved using ≥ 10mg/kg ASO compared to 3mg/kg ASO. A 50-53% decrease in GHR mRNA was observed after fourteen days of treatment at 20 and 30mg/kg ASO compared to saline and oligonucleotide controls at the same concentrations. In summary, we have demonstrated that treatment of mice with an ASO specific for the GHR suppresses serum IGF-I levels, and that this correlates with a reduction in GHR mRNA at 2 weeks and GH binding at 1 week. The reduction in serum IGF-I with ASO at 1 week was similar to that achieved with the recently approved drug Pegvisomant in a comparable mouse model. This data supports further investigations into the therapeutic potential of ASO to GHR.



#### REDUCTION IN GHR mRNA, GH BINDING AND SERUM IGF-I LEVELS IN MICE TREATED WITH GH RECEPTOR ANTISENSE OLIGONUCLEOTIDE

# George Tachas Director Drug Discovery & Patents Antisense Therapeutics ASX:ANP

2nd International GH-IGF Symposium: Cairns April 2004

## Overview: GH-IGF for growth & sight disorders

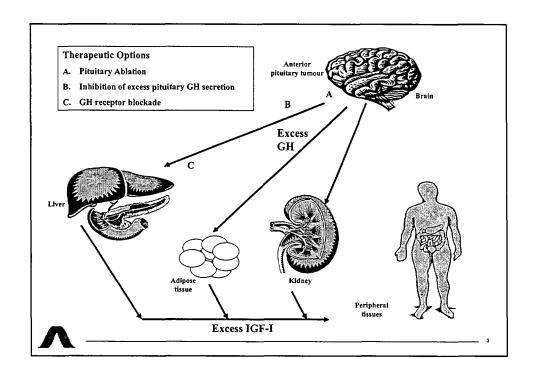
## Acromegaly

- •A disorder of excess GH in adults associated with excess sIGF-I
- •Affects 40 000 people in the US, Europe & Japan
- Pharmaceuticals:
  - Somatostatin analogues (Sandostatin<sup>TM</sup>)
- GH analogue (Trovert<sup>TM</sup>)
- •Treatment involves normalising serum IGF-I

## Diabetic Retinopathy

- •Neovascularisation of the retina leading to blindness
- •5 million Americans have diabetic retinopathy with 12-24000 new cases of blindness each year in the US
- •No drugs currently on the market:
  - · anti-VEGF & octreotide are phase III
- •Reduction of IGF-I levels is associated with clinical improvement





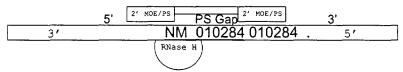
## Why use antisense oligonucleotides to GHr?

- Antisense oligonucleotide are stable & can be conveniently delivered to animals & humans
- Antisense oligonucleotides distribute unassisted to the target organs and cells
- 2<sup>nd</sup> generation antisense technology may provide clear (platform based) competitive advantages over existing treatments



## Platform features: 2nd generation antisense oligos

20 mer antisense oligo to mouse GHR also targets the GHBP



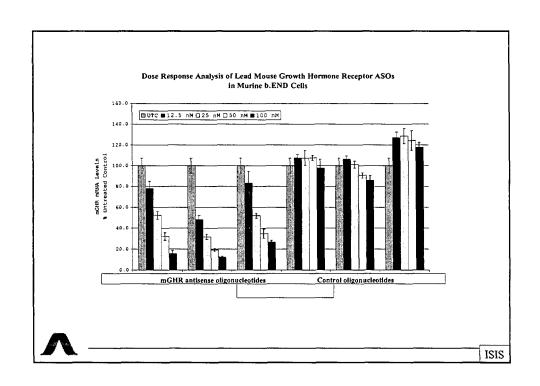
Phosphorothioate (PS) backbone throughout stabilizes oligo in vivo.

Five 2'MOE sugar modifications on the ends increases activity in vivo, dramatically increases stability (once a week dosing?), and increases oral bioavailability.

Inner PS gap region is RNase H active & directs digestion of mRNA.

Methylated cytosine bases minimize CpG effects.



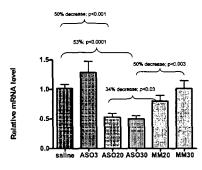


## GHR antisense: in vivo studies

- •The effect of the GHR antisense was assessed in a series of studies conducted by Prof. Mike Waters at The University Of Queensland.
- •Male Balb/c mice
- •3 weeks of age (exponential growth phase)
- •Mice were treated s.c every second day with GHR antisense or control for 7 or 14 days
- •Dose range; 3 to 50 mg/kg
- •Blood was collected and assessed for serum IGF-I levels at day 7 or 14
- •Liver tissue was collected at day 7 to determine GH binding activity
- •Liver tissue was collected at day 7 or 14 for GHR mRNA analysis



#### 2 week mouse study: GHR mRNA



Treatment Group

Relative levels of GHr mRNA detected in liver tissues collected from mice treated with GHR ASOs or mismatch oligonucleotide or saline every second day for 14 days.



Data on file

#### 2 week mouse study: sIGF-I

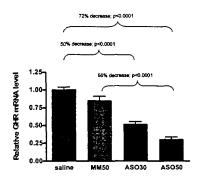
Dose (mg/kg)	Day 14 serum IGF-I (ng/ml)	% decrease relative to 3mg/kg ASO	p value
ASO 30	126	41	0.0002
ASO 20	122	43	0.0002
ASO 10	130	39	0.0002
ASO 5	194	9	0.3261
ASO 3	214	0	-

Percentage decrease in day 14 group mean serum IGF-I levels for GHR ASO treated groups relative to the GHR ASO 3mg/kg group. p values were determined by t test.



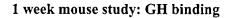
Data on file

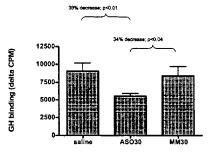
#### 1 week mouse study: GHR mRNA



Relative GHR mRNA levels detected in liver of mice treated with saline, GHR ASO at doses of 30mg/kg or 50mg/kg or mismatch delivered at 50mg/kg. Results are relative to the mean value for the saline group. Mice were treated every second day for 7 days.

Data on file





Treatment Group

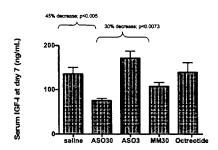
Binding of growth hormone to liver tissue collected from mice treated with either saline, GHR ASO @ 30mg/kg or mismatch oligonucleotide at 30mg/kg every second day for seven days.



Data on file

.

### 1 week mouse study: sIGF-I



Treatment Group

Serum IGF-I levels at day 7, normalised to standard control serum values. Mice were treated every second day for 7 days with either saline, GHR ASO at either 30mg/kg or 3mg/kg, or mismatch oligonucleotide at 30mg/kg. Group means +/- SEM are shown.



Data on file

#### Summary

- ASO distribute unassisted to the key organ(s) and cells
- Treatment of mice with ASO to mGHR suppresses sIGF-I at 1 and 2 weeks, and this correlates with reduction in GHR mRNA and GH binding
- · The reduction in sIGF-I at 2 weeks was dependent on dose
- ASO to mGHR produces definitive serum IGF-I suppression in male mice with up to 45% reduction at 1 week.
- Reduction in sIGF-I with ASO appears to be similar to that observed with Trovert<sup>TM</sup> (existing treatment for acromegaly) in an equivalent female mouse model (Van Neck et al; J. Endocrinol. (2000) 167, 295-303), which produced up to 49% reduction at 1 week.



13

### **Development Outlook**

- GHR is clinically validated as the best target for acromegaly & ASO distribute to key organ(s)
- If effects of ASO to GHR on sIGF-I observed in mice are reproduced in human it should provide therapeutic benefit in acromegaly and retinopathy
- Ability to test for a validated clinical endpoint in acromegaly at Phase I/IIa (<300ng/ml sIGF-I) (e.g Clemmons et al. J. Clin. Endocrinol. & Metabl. 88(10);4759)</li>
- Ability to test for validated clinical endpoint in acromegaly in short term studies;
   Effects on sIGF-I begin as early as 2 weeks with current inhibitors (Trainer et al. NEJM. April 20, 2000; 342(16):1171-7)
- ASO to GHr have potential platform based advantages over current treatments; cost, dosing route & lower frequency of dosing advantages



•

## Acknowledgements

<u>ISIS</u> <u>UQ</u> <u>ATL</u>

Brenda Baker Mike Waters Shari Lofthouse

Frank Bennett Min Rao Christopher Wraight

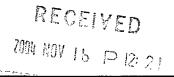
Art Levin Jega Iswaran

Mark Diamond

Kenneth Dobie Chris Belyea

Ravi Jain Mark Heffernan

A



CORPORATERIATION

Rule 4.7B

## **Appendix 4C**

## Quarterly report for entities admitted on the basis of commitments

Introduced 31/3/2000. Amended 30/9/2001

Name	of	en	tity
------	----	----	------

ANTISENSE THERAPEUTICS LIMITED

ABN

41 095 060 745

Quarter ended ("current quarter")

31 MARCH 2004

#### Consolidated statement of cash flows

Cash	flows related to	operating activities	Current quarter \$A'000	Year to date (9 months) \$A'000
1.1	Receipts from o	customers	177	879
1.2	Payments for	(a) staff costs (b) advertising and marketing (c) research and development (d) leased assets (e) other working capital *	(313) - (664) - (89)	(1,031) (1,836) (354)
1.3 1.4 1.5 1.6 1.7	received Interest and oth Income taxes p	other items of a similar nature er costs of finance paid aid details if material)	216	478 372
	Net operating	cash flows	(673)	(1,492)

<sup>\*</sup> Includes GST paid to suppliers and GST credits received from ATO.

		Current quarter \$A'000	Year to date (9 months) \$A'000
1.8	Net operating cash flows (carried forward)	(673)	(1,492)
	Cash flows related to investing activities		
1.9	Payment for acquisition of:  (a) businesses (item 5)		-
	(b) equity investments	-	
	(c) intellectual property	-	-
	(d) physical non-current assets	(2)	(10)
	(e) other non-current assets	-	- [
1.10	Proceeds from disposal of:		
	(a) businesses (item 5)	-	-
	(b) equity investments	-	-
	(c) intellectual	-	-
	property (d) physical non-	-	-
	current assets	-	-
	(e) other non-current assets	-	-
1.11	Loans to other entities	-	-
1.12	Loans repaid by other entities	-	-
1.13	Other (provide details if material)		<u> </u>
	Net investing cash flows	(2)	(10)
1.14	Total operating and investing cash flows	(675)	(1,502)
1.15	Cash flows related to financing activities Proceeds from issues of shares, options, etc.		10,396
1.16	Proceeds from sale of forfeited shares		
1.17	Proceeds from borrowings		
1.18	Repayment of borrowings		
1.19	Dividends paid		(0.0)
1.20	Other - costs relating to issue of shares		(294) 10,102
	Net financing cash flows		
	Net increase (decrease) in cash held	(675)	8,601
1.21	Cash at beginning of quarter/year to date	15,821	6,546
1.22	Exchange rate adjustments to item 1.20	-	
1.23	Cash at end of quarter	15,147	15,147

<sup>+</sup> See chapter 19 for defined terms.

## Payments to directors of the entity and associates of the directors Payments to related entities of the entity and associates of the related entities

		Current quarter \$A'000
1.24	Aggregate amount of payments to the parties included in item 1.2	123
1.25	Aggregate amount of loans to the parties included in item 1.11	-

1.26 Explanation necessary for an understanding of the transactions

Item 1.24 Reflects the following related party payments:

- (a) Total amounts paid to directors include director's fees, salaries and superannuation of \$110,686 (YTD: \$342,054).
- (b) Dr Stanley Crooke, a director of the Company is also a director of Isis Pharmaceuticals Inc ("Isis"). A total amount of \$12,476 (YTD: \$199,179) was paid to Isis for research and development related services provided by them to Antisense Therapeutics Limited ("ATL").
- (c) Professor George Werther, a director of the company, is an executive officer of the Murdoch Childrens Research Institute ("MCRI"). An amount of \$Nil (YTD: \$367,663) was paid to the MCRI for research services performed by them for ATL.

#### Non-cash financing and investing activities

2.1	Details of financing and investing transactions which have had a material effect on consolidated
	assets and liabilities but did not involve cash flows

Not applicable.			
Not applicable.			

2.2 Details of outlays made by other entities to establish or increase their share in businesses in which the reporting entity has an interest

the reporting entity has an interest	 		
Not applicable.		·	

#### Financing facilities available

Add notes as necessary for an understanding of the position. (See AASB 1026 paragraph 12.2).

		Amount available \$A'000	Amount used \$A'000
3.1	Loan facilities	-	•
3.2	Credit standby arrangements	-	-

<sup>+</sup> See chapter 19 for defined terms.

#### Reconciliation of cash

show	nciliation of cash at the end of the quarter (as n in the consolidated statement of cash flows) to elated items in the accounts is as follows.	Current quarter \$A'000	Previous quarter \$A'000
4.1	Cash on hand and at bank	2,647	3,321
4.2	Deposits at call	12,500	12,500
4.3	Bank overdraft	-	-
4.4	Other (provide details)	-	•
	Total: cash at end of quarter (item 1.23)	15,147	15,821

#### Acquisitions and disposals of business entities

		Acquisitions (Item 1.9(a))	Disposals (Item 1.10(a))	
5.1	Name of entity	Not applicable	Not applicable	
5.2	Place of incorporation or registration			
5.3	Consideration for acquisition or disposal			
5.4	Total net assets			
5.5	Nature of business			

#### Compliance statement

- 1 This statement has been prepared under accounting policies which comply with accounting standards as defined in the Corporations Act (except to the extent that information is not required because of note 2) or other standards acceptable to ASX.
- 2 This statement does give a true and fair view of the matters disclosed.

Sign here: Natalie Korchev............ Date: 29 April 2004

Company secretary

Print name: Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.

#### Notes

- 1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity wanting to disclose additional information is encouraged to do so, in a note or notes attached to this report.
- 2. The definitions in, and provisions of, AASB 1026: Statement of Cash Flows apply to this report except for the paragraphs of the Standard set out below.
  - 6.2 reconciliation of cash flows arising from operating activities to operating profit or loss
  - 9.2 itemised disclosure relating to acquisitions
  - 9.4 itemised disclosure relating to disposals
  - 12.1(a) policy for classification of cash items
  - 12.3 disclosure of restrictions on use of cash
  - 13.1 comparative information
- 3. Accounting Standards. ASX will accept, for example, the use of International Accounting Standards for foreign entities. If the standards used do not address a topic, the Australian standard on that topic (if any) must be complied with.

<sup>+</sup> See chapter 19 for defined terms.



Level 6 Central Plaza Two 66 Eagle Street Brisbane Qld 4000 GPO Box 2242 Brisbane Qld 4001 Australia

#### Facsimile transmission

Facsimil	e transmissio	'n	300	RECEIVE
Date:	14-May-2004		4.00 <b>,00</b>	- 16 PE
To:	ASX Company Ann	nouncements	1047	10 P 12:
Company:	ASX			一a Kinggig
Fax:	1900 999 279			<del></del>
CC:				
From:	Darren Mundie	Respond to:		<del></del>
Tel:	07 3360 3800	Fax:	07 3360 6622	
Pages:	4 (including this pa	ıge)		*******
Subject:	Ceasing to be a su Therapeutics Limit		der in Antisense	<del>_</del> 

#### Re: Ceasing to be a substantial shareholder in Antisense Therapeutics Limited

Please refer attached - late lodgment of Form 605 "Notice of ceasing to be a substantial holder" in Antisense Therapeutics Limited.

QIC ceased to be substantial in Antisense Therapeutics Limited on 8th October 2003 as a result of an issue of shares by the company. The increase in shares on issue was not correctly reflected in our reporting system at the time and has subsequently been amended.

Head of Investment & Portfolio Services

The information in this correspondence and any attachments are confidential. If you are not the addressee, the use or distribution of such information is prohibited. Please telephone QIC if you have received the information in error, and return the information to QIC by small, QIC will refund your costs of doing so.

Disdamer. The information in this correspondence has been prepared in good faith by Queensland Investment Corporation (QKC). However:

• QKC does not warrant the accuracy of the information, and to the extent permitted by law, disdams responsibility for any loss or damage of any nature whatsoever which may be suffered by any person directly or indirectly through relying upon it, whether that loss or damage is caused by any fault or negligence of QKC or otherwise.

• The information is not intended to constitute advice and persons should seek professional advice before relying on the information.

### Form 605

Corporations Act 2001 Section 671B

## Notice of ceasing to be a substantial holder

To Company Name / Scheme

Antisense Therapeutics Limited

ACN/ARSN

ACN 095 060 745

1. Details of Substantial Holder (1)

Name

Queensland Investment Corporation

ACN/ARSN (if applicable)

08/10/03

The holder ceased to be a substantial holder on

11/12/02

The previous notice was given to the company on

The previous notice was dated

11/12/02

#### 2. Changes in relevant interests

Particulars of each change in, or change in the nature of, a relevant Interest (2) of the substantial holder or an associate (3) in voting securities of the company or scheme, since the substantial holder was last required to give a substantial holding notice to the company or scheme are as follows:

	to change (7)	affected	

#### 3. Changes in association

The persons who have become associates (3) of, ceased to be associates of, or have changed the nature of their association (7) with, the substantial holder in relation to voting interests in the company or scheme are as follows:

Name and ACN/ARSN (if applicable)	Nature of association
N/A	

#### 4. Addresses

The addresses of persons named in this form are as follows:

Name	Address
Queensland Investment Corporation	GPO Box 2242, Brisbane QLD 4001

			e

Print name	John Gethin-Jones	Capacity	General Manager, Global Equities
Sign Here	1	Date	14 May 2009

#### Directions

- (1) If there are a number of substantial holders with similar or related relevant interests (eg. a corporation and its related corporations, or the manager and trustee of an equity trust), the names could be included in an annexure to the form. If the relevant interests of a group of persons are essentially similar, they may be referred to throughout the form as a specifically named group if the membership of each group, with the names and addresses of members is clearly set out in paragraph 4 of the form.
- (2) See the definition of "relevant interest" in sections 608 and 671B(7) of the Corporations Act 2001.
- (3) See the definition of "associate" in section 9 of the Corporations Act 2001.
- (4) Include details of
  - (a) any relevant agreement of other circumstances because of which the change in relevant interest occurred. If subsection 671B(4) applies, a copy of any document setting out the terms of any relevant agreement, and a statement by the person giving full and accurate details of any contract, scheme or arrangement, must accompany this form, together with a written statement certifying this contract, scheme or arrangement; and
  - (b) any qualification of the power of a person to exercise, control the exercise of, or influence the exercise of, the voting powers or disposal of the securities to which the relevant interest relates (indicating clearly the particular securities to which the qualification applies).

See the definition of "relevant agreement" in section 9 of the Corporations Act 2001.

- (5) Details of the consideration must include any and all benefits, money and other, that any person from whom a relevant interest was acquired has, or may, become entitled to receive in relation to that acquisition. Details must be included even if the benefit is conditional on the happening or not of a contingency. Details must be included of any benefit paid on behalf of the substantial holder or its associate in relation to the acquisitions, even if they are not paid directly to the person from whom the relevant interest was acquired.
- (6) The voting shares of a company constitute one class unless divided into separate classes.
- (7) Give details, if appropriate, of the present association and any change in the association since the last substantial holding notice.

OFFICE OF INTERCLATION OF CORPORATE FINAL CO

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

## Appendix 3B

# New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002.

Antisense Therapeutics Limited	
1	
ABN 41 095 060 745  We (the entity) give ASX the following information.	
Part 1 - All issues You must complete the relevant sections (attach sheets if there is not enough space).	
1 +Class of +securities issued or to be Ordinary Shares issued	
Number of *securities issued or to be issued (if known) or maximum number which may be issued  300	
Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)  Exercise of 300 ANPO each to purchase 300 or ANP.	

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?  If the additional securities do not rank equally, please state:  • the date from which they do  • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  • the extent to which they do not rank equally, other than in relation to the next dividend,	Yes N/A	
	distribution or interest payment		
5	Issue price or consideration	\$0.20 cents per share.	
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	Exercise of 300 ANPO 300 ordinary shares in	-
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	10 May 2004	
_		Number	+Class
8	Number and *class of all *securities quoted on ASX (including the securities in clause 2 if applicable)	355,254,050 91,467,065	Ordinary Shares (ANP) Options (ANPO)
			<u> </u>

11/3/2002 Appendix 3B Page 2

<sup>+</sup> See chapter 19 for defined terms.

9 Number and \*class of all \*securities not quoted on ASX (including the securities in clause 2 if applicable)

Number	+Class
11,500,000	Options expiring 31 July 2005 exercisable at 20 cents each (ANPAM)
20,000,000	Options expiring 30 November 2006 exercisable at 20 cents each (ANPAO)
2,450,000	Options expiring 31 July 2005 exercisable at 20 cents each (ANPAQ)

Dividend policy (in the case of a trust, distribution policy) on the increased capital (interests)

N/A

## Part 2 - Bonus issue or pro rata issue

	_	
11	Is security holder approval required?	N/A
12	Is the issue renounceable or non-renounceable?	N/A
13	Ratio in which the *securities will be offered	N/A
	•	
14	<sup>+</sup> Class of <sup>+</sup> securities to which the offer relates	N/A
15	<sup>+</sup> Record date to determine entitlements	N/A
16	Will holdings on different registers (or subregisters) be aggregated for calculating entitlements?	N/A
17	Policy for deciding entitlements in relation to fractions	N/A
18	Names of countries in which the entity has *security holders who will not be sent new issue documents	N/A
	Note: Security holders must be told how their entitlements are to be dealt with.	
	Cross reference: rule 7.7.	

<sup>+</sup> See chapter 19 for defined terms.

19	Closing date for receipt of acceptances or renunciations	N/A
20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	l '
31	How do *security holders sell part of their entitlements through a broker and accept for the balance?	

<sup>+</sup> See chapter 19 for defined terms.

32	How do *security holders dispose of their entitlements (except by sale through a broker)?	N/A
33	<sup>+</sup> Despatch date	N/A
	t 3 - Quotation of secured only complete this section if you are app	
	, , , , , , , , , , , , , , , , , , , ,	, 0, 1
34	Type of securities (tick one)	
(a)	Securities described in Part 1	
(b)		
(0)		d of the escrowed period, partly paid securities that become fully paid, when restriction ends, securities issued on expiry or conversion of
Enti	ties that have ticked box 34(	a)
	tional securities forming a new cla additional securities do not form a new clas	
Tick to docum	o indicate you are providing the informa ents	ition or
35	, ,	y securities, the names of the 20 largest holders of the e number and percentage of additional *securities held by
36		ty securities, a distribution schedule of the additional nber of holders in the categories
	1 - 1,000 1,001 - 5,000	
	5,001 - 10,000	
	10,001 - 100,000 100,001 and over	
37	A copy of any trust deed for	the additional *securities
(now g	go to 43)	

<sup>+</sup> See chapter 19 for defined terms.

Entit	ies that have ticked box 34(b)	)	
38	Number of securities for which †quotation is sought	N/A	
39	Class of *securities for which quotation is sought	N/A	
40	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	N/A	
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment		
41	Reason for request for quotation now  Example: In the case of restricted securities, end of restriction period	N/A	
	(if issued upon conversion of another security, clearly identify that other security)		
42	Number and *class of all *securities quoted on ASX (including the securities in clause 38)	Number N/A	†Class N/A

(now go to 43)

<sup>+</sup> See chapter 19 for defined terms.

#### All entities

#### Fees

3	Payment method (tick one)
	Cheque attached
	Electronic payment made  Note: Payment may be made electronically if Appendix 3B is given to ASX electronically at the same time.
	Periodic payment as agreed with the home branch has been arranged  Note: Arrangements can be made for employee incentive schemes that involve frequent issues of securities.

#### Quotation agreement

- <sup>†</sup>Quotation of our additional \*securities is in ASX's absolute discretion. ASX may quote the \*securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before 'quotation of the 'securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

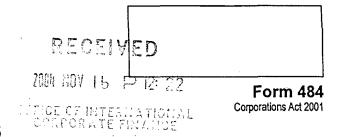
== == == == ==

Sign here: Natalie Korchev Date: 2 June 2004

Company secretary

Print name: Natalie Korchev

+ See chapter 19 for defined terms.



## Change to company details

Sections A, B or C may be lodged independently with this signed cover page to notify ASIC of:

- A1 Change of address
- A2 Change of name officeholders or members
- A3 Change ultimate holding company
- B1 Cease company officeholder
- B2 Appoint company officeholder
- B3 Special purpose company

- C1 Cancellation of shares
- C2 issue of shares
- C3 Change to share structure
- 'C4 Changes to the register of members

Refer to guide for information about  ACNJAEN  A	Company details	Gompany name
Edephore number    Concerns   Concerns   Concerns		ANTISENSE THERAPEUTICS LIMITED
Deporte key  Logs of THS  Who should ASIC contact if there is a query about this form?  Name  Na	Refer to guide for information about	ACN/ABN Corporate key
## ASIC contact if there is a query about this form?  Name    Name   Na		41 095 060 745 78841339
Name		
Name  Name  Name  Name  Name  Name  ASIC registered agent number (if applicable)  Telephone number  (O3) 9827 8999  Postal address  CCVCL 1, 10 WALLACK AVSULE  TOOLAK VIC 3142  Total number of pages including this cover sheet  Please provide an estimate of the time taken to complete this form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the atlached sections of this form are true and complete. Name  NAME CORCALV  Capacity  Director  Company secretary  Signature  N. Korchov  Date Signed  D 2 0 6 0 4	odgement details	. Who should ASIC contact if there is a query about this form?
ASIC registered agent number (if applicable)  Telephone number  (03) 9827899  Postal address  LEVEL 1, 10 WALLACK AVSUS  TOOLACK VIC 3142  Total number of pages including this cover sheet. Please provide an estimate of the time taken to complete this form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete. Name  NATAUL KORCHEV  Capacity  Director  Company secretary  Signature  N. Korchev  Date signed  D. R. O G. O G.		
Telephone number  (O3) 98278999  Postal address  LOUEL 1, 10 WALLACK AVSAUS  TOTAL number of pages including this cover sheet. Please provide an estimate of the time taken to complete this form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete. Name  NATALIS KORCHEV  Capacity  Director  Company secretary  Signature  N. Korchev  Date signed  D. 2. 0 6/0 4		NAMILLE KORCHE
Postal address  CCUSC 1, 10 WALLACK AVSUS  TOTAL number of pages including this cover sheet Please provide an estimate of the time taken to complete this fommust be signed by a current officeholder of the company.  Signature This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  NAME  VARANCE WORCHEV  Capacity  Director  Company secretary  Signature  N. Karchav  Date signed  D 2 0 6 0 0 4		ASIC registered agent number (if applicable)
Postal address  CCUCL 1, 10 WALLACK AVOUS  TOTAL number of pages including this cover sheet  Please provide an estimate of the time taken to complete this fommust be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  NAME  Capacity  Director  Company secretary  Signature  N. Karchau  Date signed  Date signed  Date signed  Date signed		
Postal address  LCUEL 1, 10 WALLACK AVAND  Total number of pages including this over sheet  Please provide an estimate of the time taken to complete this fo hrs mins  Signature This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  NATALL WORCHEV  Capacity  Director  X Company secretary  Signature  N. Korchev  Date signed  D. 2, 0 G, 0 4		
TORMY VIC 3142  Total number of pages including this cover sheet Please provide an estimate of the time taken to complete this form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  NATALE WORLHEV  Capacity  Director  Company secretary  Signature  NArcheV  Date signed  D 2 0 6 0 4		(03) 9827 8999
TOOLAKE VIC 3142  Total number of pages including this cover sheet Please provide an estimate of the time taken to complete this form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Name  Name  Capacity  Director  Company secretary  Signature  N. Kerchest  Date signed  Date signed  Date signed		Postal address
Total number of pages including this cover sheet.  Please provide an estimate of the time taken to complete this form his mins  Signature This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary  Signature  N. Karchay  Date signed  Date signed  Date signed		LEVEL 1, 10 WALLACE AVOINE
Total number of pages including this cover sheet.  Please provide an estimate of the time taken to complete this fom his mins.  Signature This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  VATAULE WORGHEV  Capacity  Director  Company secretary  Signature  N. Karchev  Date signed  D. 2, 0 6, 0 4	•	TOORAN VIC 3142
Signature This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary  Signature  N. Korchov  Date signed  D 2/0 6/0 4		
Signature This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary  Signature  N. Korckey  Date signed  D 2 10 G 0 4		
This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary  Signature  Date signed  D 2 / O G O 4		
This form must be signed by a current officeholder of the company.  I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary  Signature  Date signed  D 2 / O G O 4		
Name  Name  North Aug Vorchev  Capacity  Director  Company secretary  Signature  N. Karchev  Date signed  D 2 0 G 0 4	Signature	
Name  Name  Name  Capacity  Director  Company secretary  Signature  N. Kerchev  Date signed  D 2 0 G 0 4		officeholder of the company.
Capacity Director Signature  N. Karchav  Date signed D 2 0 G 0 4		AND A STATE OF THE PROPERTY OF A STATE OF THE STATE OF THE PROPERTY OF THE PRO
Director  Company secretary  Signature  N. Karchav  Date signed  2 0 G 0 4		I certify that the information in this cover sheet and the attached sections of this form are true and complete.
Director  Company secretary  Signature  N. Karchav  Date signed  2 0 G 0 4		I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name
Signature  N. Karchev  Date signed  D. 2. O. G. O. 4		Licertify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  NAMALE KORCHEV
Signature  N. Kerchev  Date signed  D. 2. 0 G. 0 4		Licertify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  To a complete of the attached sections of this form are true and complete.
Date signed  D 2 O G O A		I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director
Date signed  D 2 O G O A		Ceptify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary
D2/0G/04		Capacity Director  Signature
		Capacity Director  Signature
ID D M M Y		I certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary  Signature  N. Korchev
		Certify that the information in this cover sheet and the attached sections of this form are true and complete.  Name  Capacity  Director  Company secretary  Signature   N. Karchav  Date signed

Lodgement

Send completed and signed forms to:

Australian Securities and Investments Commission,

PO Box 4000, Gippsland Mail Centre VIC 3841.

Or lodge the form electronically by visiting the ASIC website www.asic.gov.au

For help or more information

Telephone 03 5177 3988

Email

info.enquiries@asic.gov.au

Web

www.asic.gov.au

C1 Cancellation of shares	
Reason for cancellation Please indicate the reason that shares	Redeemable preference shares—S:254J
have been cancelled (select one or more boxes)	Redeemed out of profits
,	Receimed out of proceeds of a fresh issue of shares
· 	Capital reduction — S:256A—S:256E
:	Single shareholder company
	Multiple shareholder company. A Form 2560 must be lodged before a capital reduction takes place
	Share buy back — \$\$.257H(3)
	Minimum holding buy-back by listed company
	Other buy-back type: A form 280 or 281 must be lodged at least 14 days, and no more than 1 year before the share buy-back can take place
	Forfeited shares — \$.258D
	Increited shares — \$.2580  Shares returned to a public company — \$\$.258E(2) & (3)
: :	Under section 651C, 724(2), 737 or 738
	Under section 1325A (court order)
	Other Description
•	Give section reference
Details of cancelled shares	List the details of shares cancelled in the following table  Share class code: Number of shares cancelled: Amount paid (cash or otherwise):
4	Earliest date of change
	Please indicate the earliest date that any of the above changes occurred.
	D D/M M/N Y

iare class code	Number of shares issued Amount	paid per share	Amount unpaid per share	9
ORO	300	20 cents	Nil	
	earliest date that any of the above changes occurred			
Yes  if yes, propriand either a  No if no, propris	etary companies must also lodge a Form 2072 certifying the Form 208 or a copy of the contract.  Itary companies are not required to provide any further documents to share structure  to share structure table has occurred (eg. as a result of the is	at all stamp duties have been paid. If	iles must also lodge a Form	208.
Yes fryes propr and either a  No frino, proprii  Change e a change to thed. Details of si	etary companies must also lodge a Form 2072 certifying tha Form 208 or a copy of the contract.  Itary companies are not required to provide any further docu	at all stamp duties have been paid. If ments with this form, Public comparates with this form, Public comparates or cancellation of shares), plea	iles must also lodge a Form se show the updated details Total amount paid on these	208.
Yes  if yes, propriand either a  No  if no, proprie  Change re a change to to	etary companies must also lodge a Form 207Z certifying the Form 208 or a copy of the contract.  Itary companies are not required to provide any further documents of the structure and the structure table has occurred (eg. as a result of the is hare classes not affected by the change are not required here	at all stamp duties have been paid. If ments with this form, Public compar ssue or cancellation of shares), plea a. Total number of shares (current after changes)	iles must also lodge a Form se show the updated details Total amount paid on these	s for the share of Total amount unpaid on thes
if yes propriand either a No fro, proprie e a change to the ded. Details of signals code.	etary companies must also lodge a Form 207Z certifying the Form 208 or a copy of the contract.  Itary companies are not required to provide any further documents of the structure as the structure table has occurred (eg. as a result of the is hare classes not affected by the change are not required here.  Full title if not standard.	ments with this form. Public comparessue or cancellation of shares), please.  Total number of shares (current after changes)	se show the updated details  Total amount paid on these shares	s for the share of total amount unpaid on thes shares

Lodgement details

is this document being lodged to update the Annual Company Statement that was sent to you?

Yes

No

#### C4 Changes to the register of members Use this section to notify changes to the register of members for your company (changes to the shareholdings of members): If there are 20 members or less in a share class, all changes need to be notified If there are more than 20 members in a share class, only changes to the top twenty need be notified (\$178B) If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned The changes apply to Family name Given names Please indicate the name and address of the member whose shareholding has changed OR Company name ACN/ARBN/ ABN Office, unit, level, or PO Box number Street number and Street name State/Territory Country (if not Australia) Date of change Earliest date of change Please indicate the earliest date that any of the following changes occurred. [M M] The changes are Share class Shares Shares \*Total \$ Total number. \*Total \$ paid Fully paid Beneficially: Top 20 decreased by code increased by now held on these unpaid (y/n)\_ held (y/n) member (y/n) ... (number) , (number) on these shares shares

\*Public companies are not required to provide these details

Date of entry of member's name in register

(New members only)

	Date	of	ent	ŢΫ				5.1	Ki		[]. [].		7				37			Δï		H				17	13	W		Tipp.	MĘ	
		Г	٦	ŕ	٦		٦,	Γ	٦	3.11	1	i d di	Ę.		10	<u>, i i</u>				Ďij,		ig in Notice Notice	in.		Ţ				49		4,40 34,40	
١		Ļ	ال				۱,					î.	r î;			ara Tan		in ya Milet				4		H			M	iĮ,				Ä
Į.	D		D]	[]	1	M	J.	ĮΥ	M.	Y		'n				e i i Lai		janaj Hana		1.16												Ø

ASIC Form 484 26 February 2004 Section C Page 4 of 5

# C4 Continued... Further changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

• If there are 20 members or less in a share class, all changes need to be notified

- If there are more than 20 members in a share class, only changes to the top twenty need be notified (\$178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to Please indicate the name and address of the member whose shareholding has	Family I	name	G J	ven names			
changed	OR Compa	ny name					
	ACN/ARBN//	ABN svel, or PO Box r	ilmher.				
		r and Street nan					
	Suburb/City					State/I	
	Postcode		Country (if not	Australia)			
Earliest date of change Please indicate the earliest date that any of the following changes occurred.  The changes are	Date of chan		n				
Share class Shares Si code increased by de		Total number : now held	*Total \$ paid = on these shares	*Total \$ unpaid on these shares	Fully paid (y/n)	Beneficially held (y/n)	Top 20 member (y/n)
*Public companies are not required to pro							
Date of entry of member's name in register (New members only)	Date of enti		M				



RECEIVED

200 101 15 P 10 22

7 June 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Presentation - BIO2004 Annual International Convention

Antisense Therapeutics Limited has been invited to present at the BIO2004 Annual International Convention, which takes place June 6-9, 2004 in San Francisco. With respect thereto, please find enclosed a copy of the company's presentation.

Yours sincerely

Natalie Korchev Company Secretary



# ANTISENSE THERAPEUTICS

# **ASX:ANP**

June 2004

# **Antisense Therapeutics Ltd**

- •Listed on ASX Dec 2001
- •Total funds raised to date: A\$28.5 M
- •Market Cap: A\$44 M
- Key Shareholders
  - •Circadian 20.4%
  - •Syngene 15.3% (42% Circadian)
  - •lsis 11.3%
  - •QIC 4.5%
- •Cash reserves of A\$14 M, no borrowings

A

#### **Board of Directors**

- •Bob Moses, Chairman (ex VP of CSL)
- Mark Diamond, CEO (ex Faulding)
- •Dr Chris Belyea (CEO Metabolic)
- •Dr Stanley Crooke (Founder ISIS Pharmaceuticals, Inc)
- Prof Graham Mitchell (Foursight/CSL)
- Prof George Werther (Murdoch Childrens Research Institute)



#### **ANP's Mission**

- •Create, develop and commercialize novel antisense pharmaceuticals for large and/or niche unmet markets
- •Select targets where our technology will provide clear competitive advantages



#### **Business strategy**

- Leverage 14 years of Isis antisense technology development
- •Fast track existing lead projects through pre-clinical and clinical development
- •Create pipeline of new antisense therapeutics
- •Commercialise those that are successful in clinical testing via licensing/partnering



# Strategic Partner ISIS Pharmaceuticals Inc

- Acknowledged global leader in antisense
- •Over US \$1B invested in antisense chemistries
- •More than 1,000 patents issued
- •1 FDA drug approved, 7 in late stage clinical development
- •Deals with large market cap companies (eg Lilly and Amgen)

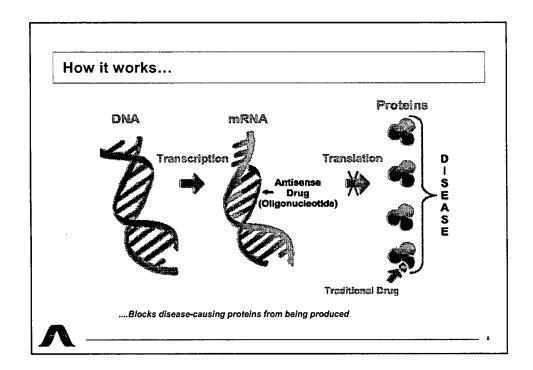


## What is antisense technology?

A fundamentally different approach to making medicine:

- Unprecedented target specificity and selectivity
- •Most current drugs interfere with the activity of proteins that cause disease
- •Antisense drugs go to work earlier, they block the manufacture of the target protein



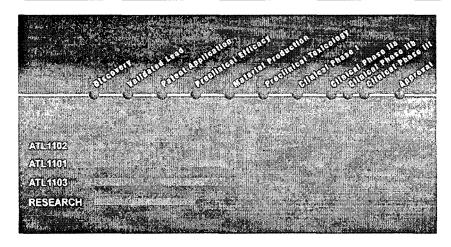


## Technical advantages

- Mature technology (20 years in development)
- •Drug discovery and research is faster and more predictable
- •Compounds are potentially more selective, effective and less toxic
- •Broad disease application
- Dosing advantages (route and frequency)



# **Development Pipeline**



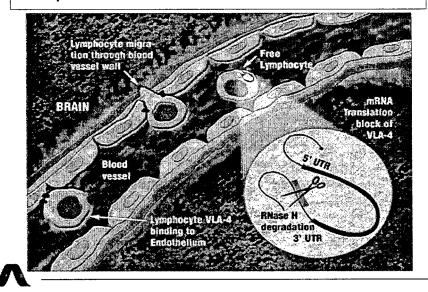


- •MS is a progressive neurological disease
- •Onset of MS is usually at young age (20 -40 years)
- •MS affects 2.5 million people world-wide
- •No cure; drugs aim to delay disease progression
- •Beta-interferon (1a, 1b) leading therapy
  - Biogen, Serono, Schering AG
- •Need for more effective drugs with less side effects
- •Global drug sales for MS >US\$ 2.5 billion in 2003



11

## Multiple sclerosis - ATL1102



## **Product**

- Antisense inhibitor to VLA-4 protein which contributes to onset of disease
- Confirmed activity in pre-clinical mouse model of MS (also other inflammatory disorders asthma & arthritis)



13

## Multiple Sclerosis - ATL1102

# Product (cont)

VLA-4 is a validated target

- Biogen Idec's Antegren<sup>™</sup> (also targets VLA-4) in Phase III trials:
  - Marketing application filed with FDA based on interim 1 year phase III data\*
  - Provides greater confidence in likelihood of clinical success of ATL1102
  - Anticipate efficacy, dosing and cost advantages with ATL1102



Problems with Current Therapies*	In Development Antegren*	ATL1102
Partial or no response to βIFNs & Copaxone	Different mechanism of action	Different mechanism / no neutralising antibodies
Flu-like symptoms	No flu-like symptoms	No flu-like symptoms
Dosing too frequent	Only 1x/month	Dosing TBC – potentially 1x/week or 1x/month
Don't want injection responsibility / inconvenience	IV done by doctor	Sub-cutaneous, potential needless injection/oral



Source: Biogen website – The JP Morgan 21st Annual Healthcare Conference Presentation (14/1/03)

..

# Multiple Sclerosis - ATL1102

# **Progress**

- Manufactured drug product for Phase I and IIa studies
- Phase I human trial underway dosing completed
- Preliminary results presented at Australian Neurosciences Conference in January '04



## Outlook

- Phase I trial final reports due mid '04
- Following successful completion of Phase I trial company will make an application for the Phase IIa patient trial
- Phase IIa trials scheduled to commence in 2nd half 2004



17

#### **Psoriasis Treatment - ATL1101**

#### Disease & Market

- Chronic non-contagious skin disorder
- Affects 1-2% of population
- Global drug sales forecast to exceed US\$2 billion by 2007 (Frost & Sullivan)
- Need for more effective therapies

#### Product

- Antisense inhibitor to IGF-IR regulates cell growth
- Developing topical formulation



#### **Psoriasis Treatment - ATL1101**

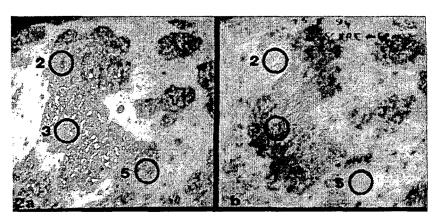
# **Progress**

- · Completed pre-clinical efficacy program
- Awarded A\$1.1 million government grant
- "Proof of Concept" (PoC) study in psoriasis patients
  - •Manufacture of compound for study underway
  - Commenced animal toxicology program



19

#### Human proof of concept strategy - Psoriasis small plaque assay



Rappersberger et al., Clearing of psoriasis by a novel immunosuppressive macrolide. J Invest Dermatol 106, 701-10 (1996).

A

#### **Psoriasis Treatment - ATL1101**

## Outlook

 Commence PoC trial in 2nd half 2004 after toxicology studies successfully completed and relevant approvals received



\_ 21

## **Research Pipeline**

- •Projects that target diseases of growth, vision and major inflammatory diseases
- •Animal studies are at various stages of completion
- •Most advanced research pipeline project: ATL1103 for growth & sight disorders
- •Project to move into development



# Growth - Acromegaly

- The Disease
  - •A disorder of excess growth hormone in adults associated with excess serum IGF-1
  - •Affects 40,000\* people
- The Market
  - •High treatment costs (from A\$14K-\$33K/annum)
  - •Somatostatin analogue effective in ~ 60% of patients
  - •TrovertTM sales projected to reach US\$500 million



\* US, Europe and Japan

23

## ATL1103 for growth & sight disorders

# Sight - Diabetic Retinopathy

- The Disease
  - Neovascularisation of the retina leading to blindness
  - •High prevalence: over 5 million Americans affected by diabetic retinopathy
  - •12,000-24,000 new cases of blindness per year in US
- The Market
  - •No approved drug treatments for diabetic retinopathy
  - •\$Billion market potential



## **Product**

- Antisense inhibitor to the GH receptor
- GH action is mediated through IGF-1 hormone
- Acromegalics have elevated levels of both GH and IGF-1
- Acromegaly treatment involves normalising IGF-I levels
- Reduction of IGF-I levels is associated with clinical improvement in retinopathy



- 25

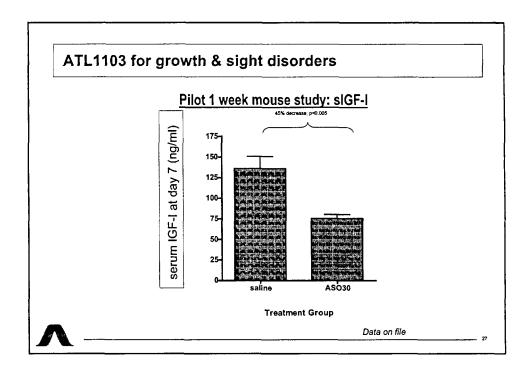
#### ATL1103 for growth & sight disorders

# Results of Animal Studies

- IGF-1 suppression by ATL1103 comparable to TrovertTM (existing treatment for acromegaly) in an equivalent mouse model
- Data presented at 2nd International Symposium on GH & IGF-I, Cairns, Australia, April 2004
- Patent applications filed



:5



# Why ATL1103?

- · Consistent with and validates ATL business plan
  - •Grow business and diversify risk through product pipeline development
- Attractive Project
  - ·Significant market potential
  - •GHr target is clinically validated
  - •Ability to test for clinical endpoint (serum IGF-I) in early human studies
  - Limited competition
  - •Potential dosing, administration and cost advantages

Λ

# Competitor drugs in acromegaly

Drug	Efficacy	Route	Dosing Frequency	Cost (A\$)
GHr antagonist  Trovert <sup>TM</sup>	90-95%	sc	1 x per day	\$20-25,000/yr estimated
Somatostatin analogues (octreotide)				
Sandostatin™ Sandostatin LAR™	65% 65%	sc im depot	3 x per day 1 x per month	\$14 -33,000/yr*
Dopamine agonists				
Parlodel™ Dostinex™	10% >10%	oral oral	4 x per day 2 x per week	



Annual treatment costs vary depending on dosage and frequency from A\$14-33,000 per patient/year.

29

# ATL1103 for growth & sight disorders

# Outlook

• Place order for bulk drug product to commence preclinical safety studies



#### Outlook

Project	Value Driver	Timing
ATL1102	•Complete Phase I	1st half '04
MS	•Start Phase IIa	2 <sup>nd</sup> half '04
	•Partnering objective	Concl Ph Ila
ATL1101 Psoriasis	Complete product manufacture and toxicology program	1st half '04
	•Start "Proof of Concept" study	2 <sup>nd</sup> half '04
	•Partnering objective	Concl "PoC"
ATL1103 Acromegaly	Commence product manufacture for pre-clinical toxicology	1 <sup>st</sup> half04



4

## **ANP – Investment Fundamentals**

#### Attractive product pipeline

- · Validated targets (lower development risk)
- Products with platform based competitive advantages
- Significant market potential

#### Track record for hitting development milestones

- Mature, efficient, and predictable platform technology
- High quality and effective collaborations (Isis/MCRI)
- Experienced management team

## Clear commercialisation objectives

## Near term key value drivers

· ATL1102 & ATL1101 in patient trials in '04



The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

#### Stock Exchange Announcement 8 June 2004

#### ANTISENSE THERAPEUTICS LIMITED AND ISIS PHARMACEUTICALS ANNNOUNCE POSITIVE RESULTS FROM A PHASE 1 TRIAL OF ATL-1102 FOR MULTIPLE SCLEROSIS

Please find attached a joint announcement by Antisense Therapeutics Limited and Isis Pharmaceuticals Inc for release to the market regarding positive results from a Phase 1 trial of ATL-1102 for Multiple Sclerosis. This announcement is being conjointly released in the US.

Yours sincerely

Natalie Korchev Company Secretary

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999 Contact: Kristina Peterson

Isis Pharmaceuticals

760-603-2521

Natalie Korchev

Antisense Therapeutics Limited

+61 3 9827 8999

#### ANTISENSE THERAPEUTICS LIMITED AND ISIS PHARMACEUTICALS ANNOUNCE POSITIVE RESULTS FROM A PHASE 1 TRIAL OF ATL-1102 FOR MULTIPLE SCLEROSIS

ATL expects to start Phase 2 studies of ATL-1102 in patients with MS this year

Melbourne, Australia and Carlsbad, CA, USA, June 8, 2004 – Antisense Therapeutics Limited (ASX: ANP) and Isis Pharmaceuticals, Inc. announced today the results of a dose-escalating Phase 1 study of ATL-1102. Based on the study's results 6 mg/kg/week of ATL-1102 appeared well-tolerated and has been selected as the proposed dose for Phase 2 development. A Phase 2 clinical trial is expected to begin in the second half of 2004. ATL-1102 is a second-generation antisense inhibitor of VLA-4 (Very Late Antigen-4). Inhibition of VLA-4 has been shown to have positive effects in multiple animal models of inflammatory diseases, including MS.

"We are pleased with the favorable results of this trial which, along with preclinical data, give us critical dose information allowing us to move confidently to the next stage of clinical development," said Mark Diamond, Antisense Therapeutics, Chief Executive Officer.

The double-blind, randomized, dose-escalation, placebo-controlled Phase 1 study evaluated the pharmacokinetic and safety profile of ATL-1102. In 54 healthy volunteers, ATL-1102 was either delivered in an intravenous (IV) or subcutaneous (SQ) formulation. ATL-1102 was well-tolerated. The most frequently reported side effects included mild "flu-like" symptoms and occasional injection site reactions, which were generally mild and increased in incidence and severity with escalating dose levels, particularly at 12 and 18 mg/kg/week. The trial was conducted at the Charterhouse Clinical Research Unit of the Ravenscourt Park Hospital (formerly Stamford Hospital) in London.

"These data are consistent with the results of other second-generation antisense drugs demonstrating the predictability of the antisense platform," said Stanley T. Crooke, M.D., Ph.D., Chairman and Chief Executive Officer of Isis Pharmaceuticals. "We continue to make excellent progress with our second-generation antisense drugs with results announced from three trials so far this year and we expect to continue that clinical momentum throughout 2004."

Antisense Therapeutics is in the process of preparing an application to conduct a Phase 2a clinical trial in MS patients. The trial is expected to be conducted in Europe and the clinical trial application will be filed with an appropriate European regulatory authority. Regulatory agency approval and commencement of the Phase 2a trial are expected to occur during the second half of this year.

#### **Background Information**

Multiple Sclerosis (MS) is a life-long chronic, incurable disease that progressively destroys the central nervous system. It is commonly diagnosed between the ages of 20 and 40 years. According to the National Multiple Sclerosis Society, MS is an autoimmune disease that affects the central nervous system (CNS). Approximately 400,000 Americans acknowledge having MS, and every week about 200 individuals are diagnosed. Worldwide, MS may affect more than two million people.

ATL-1102 is an inhibitor of CD49d, a sub-unit of VLA-4 (Very Late Antigen-4). In MS, white blood cells (leukocytes) are pulled into the CNS from the blood. The inhibition of VLA-4 may prevent white blood cells from entering the CNS to stop the progression of MS. Inhibition of VLA-4 in animals has demonstrated positive effects on a number of inflammatory diseases such as MS. Several other VLA-4 inhibitors are in clinical development for inflammatory conditions. Isis discovered this compound and licensed it to Antisense Therapeutics Limited in 2001.

Antisense Therapeutics Limited is an Australian publicly listed biopharmaceutical drug discovery and development company (ASX: ANP). ANP's mission is to create, develop and commercialize novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL-1102), and Psoriasis (ATL-1101). ANP plans to commercialize its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies. The company's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals, Inc., Queensland Investment Corporation and the Murdoch Childrens Research Institute. Further company details are available on the Antisense Therapeutics website at www.antisense.com.au.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and its partners. The company has successfully commercialized the world's first antisense drug and has 11 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and is discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,300 issued patents worldwide. Additional information about Isis is available at <a href="https://www.isispharm.com">www.isispharm.com</a>.

This press release includes forward-looking statements regarding Isis' collaboration with Antisense Therapeutics and the development, therapeutic potential and safety of ATL-1102 (ISIS 107248) targeting VLA-4 and in treating multiple sclerosis. Any statement describing our goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology and systems used to identify infectious agents, in discovering and commercializing drugs that are safe and effective for use as human therapeutics and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this press release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in Isis' Annual Report on Form 10-K for the year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended March 31, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

Ibis Therapeutics® is a registered trademark of Isis Pharmaceuticals, Inc.

# # #

MINOY 16 P 12: 22

Rule 3.19A.2

# CORPORATE Appendix 3Y

# **Change of Director's Interest Notice**

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 30/9/2001.

Name of entity:	Antisense Therapeutics Limited	
ABN:	41 095 060 745	

We (the entity) give ASX the following information under listing rule 3.19A.2 and as agent for the director for the purposes of section 205G of the Corporations Act.

Name of Director	George A Werther
Date of last notice	4 January 2002

#### Part 1 - Change of director's relevant interests in securities

In the case of a trust, this includes interests in the trust made available by the responsible entity of the trust

Note: In the case of a company, interests which come within paragraph (i) of the definition of "notifiable interest of a director" should be disclosed in this part.

Direct or indirect interest	Direct	
Nature of indirect interest (including registered holder) Note: Provide details of the circumstances giving rise to the relevant interest.		
Date of change	4 June 2004	,
No. of securities held prior to change	25,000 12,500 2,000,000	ordinary shares fully paid options expiring 1/2/07 exercisable at 20 cents each options expiring 31/7/05 exercisable at 20 cents each
Class	Fully paid c	ordinary shares
Number acquired	1,687,500	· · · · · · · · · · · · · · · · · · ·
Number disposed	-	
Value/Consideration  Note: If consideration is non-eash, provide details and estimated valuation	\$12,993.7	75

<sup>+</sup> See chapter 19 for defined terms.

No. of securities held after change	1,712,500 ordinary shares fully paid 12,500 options expiring 1/2/07 exercisable at 20 cents each			
	2,000,000	options expiring 31/7/05 exercisable at 20 cents each		
Nature of change Example: on-market trade, off-market trade, exercise of options, issue of securities under dividend reinvestment plan, participation in buy-back		transaction through exercise of an eement: - See part 2 below for ils.		

# Part 2 - Change of director's interests in contracts

Note: In the case of a company, interests which come within paragraph (ii) of the definition of "notifiable interest of a director" should be disclosed in this part.

Detail of contract	Option Agreement between Murdoch Children's Research Institute (MCRI) and George Werther.
Nature of interest	George Werther had an option agreement with the MCRI to purchase 1,687,500 ordinary shares in Antisense Therapeutics.
Name of registered holder (if issued securities)	See above.
Date of change	George Werther submitted an application in May 2004 to exercise his options under the agreement to acquire 1,687,500 ordinary shares in Antisense Therapeutics from the MCRI.  The date of entering these securities into uncertificated holdings was on 4 June 2004.
No. and class of securities to which interest related prior to change  Note: Details are only required for a contract in relation to which the interest has changed	
Interest acquired	On the exercise of the option under the agreement, 1,687,500 ordinary shares in Antisense Therapeutics were acquired.
Interest disposed	The option agreement now ceases to exist.
Value/Consideration Note: If consideration is non-cash, provide details and an estimated valuation	See Part 1 above.
Interest after change	The option agreement now ceases to exist. For number of securities held by George Werther after the change see Part 1 above.

<sup>+</sup> See chapter 19 for defined terms.

Appendix 3Y Page 2

11/3/2002



1 July 2004

# Investor Update – Market Developments re Treatments for Multiple Sclerosis

As previously advised by Antisense Therapeutics in its March 2004 Investor Update, US biotech company BioGen Idec and its partner Elan Corporation announced earlier in the year their intention to file their Multiple Sclerosis drug, Antegren®, with the US Food and Drug Administration. In May 2004, these companies filed their Biologics License Application with the FDA.

On Monday US time, Biogen and Elan announced that "the Biologics License Application (BLA) for Antegren® (natalizumab) has been designated for Priority Review and Accelerated Approval by the U.S. Food and Drug Administration (FDA) for the treatment of multiple sclerosis. The next step in the process is action by the FDA on formal acceptance of the application which occurs within 60 days of submission.

The FDA grants Priority Review status to products that are considered to be potentially significant therapeutic advancements over existing therapies that address an unmet medical need. Based on the FDA's designation of Priority Review for natalizumab in MS, the companies anticipate action by the Agency approximately six months from the submission date, rather than 10 months for a standard review."

Elan (ELN:NYSE) and Biogen Idec (BIIB: Nasdaq) respective share prices increased on the release of this news.

The FDA's review of Biogen/Elan's BLA "will be based on one-year data from two ongoing Phase III studies." Whilst the results have not been released, commentators have interpreted the early submission of the BLA with the FDA as a positive indication of the likelihood of success of the drug in the clinic.

#### Positive impact on ATL1102 for multiple sclerosis

So how does this impact on Antisense Therapeutics, and more particularly, the development of its own MS drug, ATL1102?

As stated in the company's March 2004 Investor Update, both Antegren® and Antisense Therapeutics' MS compound ATL1102 target the VLA-4 protein (Alpha-4 integrin chain), which is considered to be responsible for the progression of MS.

ATL1102 is a second-generation antisense drug designed to act at an earlier stage of the disease process (than Antegren®) by preventing excessive amounts of VLA-4 being

produced. ATL1102 may also provide important advantages over Antegren®, in particular the cost of therapy and method of delivery, as well as improved effectiveness.

The recent Antegren® news provides Antisense Therapeutics with greater confidence in the likely success of ATL1102. Also, the submission of the Antegren® application to the FDA will establish a path to regulatory approval for ATL1102 and commercially and scientifically validate the company's MS drug development strategy.

Antisense Therapeutics, which reported positive results from a Phase I trial of ATL1102 earlier this month, is in the process of preparing an application to conduct a Phase IIa clinical trial of this compound in MS patients. Regulatory agency approval and commencement of the Phase IIa trial are expected to occur during the second half of this year.

It is the company's understanding that, with the exception of Antegren®, there are no other drugs that specifically target VLA-4 in clinical trials in patients with MS. Antisense Therapeutics has a worldwide exclusive license to ATL1102 from Isis. Isis has US granted patents and other pending patent rights over antisense drugs targeting VLA-4. Non-antisense methods of regulating VLA-4 activity are believed to infringe Elan's US patent over Antegren® licensed exclusively to Biogen. This should reduce the likelihood that Antisense Therapeutics and Elan/Biogen Idec will be joined by other competitors with MS treatments targeting VLA-4.

#### About Antisense Therapeutics Limited

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS) and Queensland Investment Corporation.

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999 2001 NOV 14 P 12: 22

OFFICE OF INTERRATE COMPORATE FOR IT

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

# Appendix 3B

# New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002, 1/1/2003.

Name	of entity	
ANT	ISENSE THERAPEUTICS LIMITI	ED
ABN 41 09	95 060 745	
We (	the entity) give ASX the following i	information.
	rt 1 - All issues nust complete the relevant sections (attach s	heets if there is not enough space).
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	Ordinary Shares
2	Number of *securities issued or to be issued (if known) or maximum number which may be issued	1,200
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	Exercise of 1,200 ANPO options at \$.20 cents each to purchase 1,200 ordinary shares in ANP.

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	Yes	
	If the additional securities do not rank equally, please state:  • the date from which they do  • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
5	Issue price or consideration	\$0.20 cents per share.	
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	Exercise of 1,200 ANF 1,200 ordinary shares in	
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	17 June 2004	
		Number	+Class
8	Number and *class of all *securities quoted on ASX (including the securities in clause 2 if applicable)	355,255,250 91,465,865	Ordinary shares (ANP) Options (ANPO)

Appendix 3B Page 2

<sup>+</sup> See chapter 19 for defined terms.

9 Number and \*class of all \*securities not quoted on ASX (including the securities in clause 2 if applicable)

Number		+Class
11,	500,000	Options expiring 31 July 2005 exercisable at 20 cents each (ANPAM)
20,	,000,000	Options expiring 30 November 2006 exercisable at 20 cents each (ANPAO).
2	,450,000	Options expiring 31 July 2005 exercisable at 20 cents each (ANPAQ)

Dividend policy (in the case of a trust, distribution policy) on the increased capital (interests)

N/A		

# Part 2 - Bonus issue or pro rata issue

11	Is security holder approval required?	N/A
12	T. A. ( 1	NT/A
12	Is the issue renounceable or non-renounceable?	N/A
13	Ratio in which the *securities will be offered	N/A
14	<sup>+</sup> Class of <sup>+</sup> securities to which the offer relates	N/A
15	<sup>+</sup> Record date to determine entitlements	N/A
16	Will holdings on different registers (or subregisters) be aggregated for calculating entitlements?	N/A
17	Policy for deciding entitlements in relation to fractions	N/A
18	Names of countries in which the entity has *security holders who will not be sent new issue documents	N/A
	Note: Security holders must be told how their entitlements are to be dealt with.	
	Cross reference: rule 7.7.	
10		Esv.
19	Closing date for receipt of acceptances or renunciations	N/A

1/1/2003

Appendix 3B Page 3

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a broker and accept for the balance?	N/A

<sup>+</sup> See chapter 19 for defined terms.

		_
32	How do *security holders dispose of their entitlements (except by sale through a broker)?	'A
33	*Despatch date N	'A
	rt 3 - Quotation of securiting and only complete this section if you are applying	
34	Type of securities (tick one)	
(a)	Securities described in Part 1	
(b)	All other securities	
		escrowed period, partly paid securities that become fully paid, employee securities issued on expiry or conversion of convertible securities
Enti	tities that have ticked box 34(a)	
Addi	litional securities forming a new class	of securities
Tick t docun	to indicate you are providing the information ments	or
35		curities, the names of the 20 largest holders of the mber and percentage of additional *securities held by
36	If the *securities are *equity s *securities setting out the number 1 - 1,000 1,001 - 5,000 5,001 - 10,000 10,001 - 100,000 100,001 and over	ecurities, a distribution schedule of the additional of holders in the categories
37	A copy of any trust deed for the a	dditional †securities
+ See	ee chapter 19 for defined terms.	

1/1/2003

# Entities that have ticked box 34(b)

38	Number of securities for which †quotation is sought	N/A	
39	Class of *securities for which quotation is sought	N/A	
40	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?  If the additional securities do not rank equally, please state:  • the date from which they do  • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
41	Reason for request for quotation now	N/A	
	Example: In the case of restricted securities, end of restriction period		
	(if issued upon conversion of another security, clearly identify that other security)		
	•		
		Number	+Class
42	Number and *class of all *securities quoted on ASX (including the securities in clause 38)	N/A	N/A

Appendix 3B Page 6

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

#### Quotation agreement

- †Quotation of our additional \*securities is in ASX's absolute discretion. ASX may quote the \*securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will not require disclosure under section 707(3) or section 1012C(6) of the Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before †quotation of the †securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here:

Natalie Korchev

Date: 9 July 2004

Company secretary

Print name:

Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.

2004 NOV 15 P 12: 22

**Form 484** 

Corporations Act 2001

# Change to company details

OFFICE OF INTERMATION :--

Sections A, B or C may be lodged independently with this signed cover page to notify ASIC of:

- A1 Change of address
- A2 Change of name officeholders or members
- A3 Change ultimate holding company
- B1 Cease company officeholder
- B2 Appoint company officeholder
- B3 Special purpose company

- C1 Cancellation of shares
- C2 Issue of shares
- C3 Change to share structure
- C4 Changes to the register of members

Company details	Company name
	ANTISONSE THERAPENTICS LIMITED
Refer to guide for information about corporate key	ACN/ABN Corporate key 740 095 060 745 788 41 339
_odgement details	Who should ASIC contact if there is a query about this form?
	Name NATALIE KORCHEV
	ASIC registered agent number (if applicable)
	Postal address  LEVEC   10 WALLACE ANSWE
	1000AK NC 3142
	Total number of pages including this cover sheet Please provide an estimate of the time taken to complete this form  his mins
Signature	
This form must be signed by a current	Lecritify that the information in this cover sheet and the attached sections of this form are true and complete.
	NAME NAMALIE WORCHEV
	Capacity Director
	Director  X Company secretary
	Director:

Lodgement

Send completed and signed forms to:

Australian Securities and Investments Commission,

PO Box 4000, Gippsland Mail Centre VIC 3841.

Or lodge the form electronically by visiting the ASIC website www.asic.gov.au

For help or more information

Telephone 03 5177 3988

Email

info.enquiries@asic.gov.au

Web

www.asic.gov.au

# Section C completion guide

# Standard share codes

Refer to the following table for the share class codes for sections C1, C2, C3 and C4

Share class code Full title		Share class code	Full title
A	A	La PRE C	preference
B	Betc	CUMP	cumulative preference
EMP	employee's	NCP	non-cumulative preference
FOU:	founder's	REDP	redeemable preference
1G -	life governor's	NRP	non-redeemable preference
MAN	management	CRP	cumulative redeemable preference
ORD	ordinary	NCRP	non-cumulative redeemable preference
RED	redeemable	PARP	participative preference
SPE	special		

If you are using the standard share class codes you do not need to provide the full title for the shares, just the share class code.

If you are not using the standard share class code, enter a code of no more than 4 letters and then show the full title,

## Sections to complete

Use the table below to identify the sections of this form to complete (please indicate the sections that have been completed). Completion of this table is optional.

	C1 - Cancellation of shares	G2 - Issue of shares	C3 - Change to share structure table	C4 - Change to members register
Issue of shares				
Propnetary company	Not required.	1		17
Public company				
	Not required	1/	Z-C	1
if not in response to the Annual company statement	Not required +		Not required	Not required
Cancellation of shares				
Proprietary company	1	Not required	1/	V
Public company				
If in response to the Annual company statement		Not required		1
If not in response to the Annual company statement		Not required	Not required:	Not required .
Transfer of shares				
Proprietary company	Not required	Nat required	Not required	<b>V</b>
Public company				
f in response to the Annual company statement	Not required	Not required	Not required :	
finct in response to the Annual company statement	Not required	Not required	Not required	Not required
Changes to amounts paid				
Proprietary company	Not required	Not required		
Public company				
f in response to the Annual company statement	Not required:	Not required		
f not in response to the Annual company statement	Not required	Notirequired	Not required -	Not required
every. Changes to beneficial ownership				
Proprietary company	Not required	Not required	Not required	
Public company				
if in response to the Annual company statement	Not required	Not required	Not required	
if not in response to the Annual company statement	Not required	Not required	Not required	Not required

To notify ASIC about a division or conversion of a class of shares, you must lodge a form 211 within 28 days of the change occurring.

To notify ASIC about a conversion of shares into larger or smaller numbers, you must lodge a form 2205B within 28 days of the change occurring.

# C1 Cancellation of shares

Reason for cancellation Please indicate the reason that shares have been cancelled (select one or more boxes)	Redeemable preference shares — S.254J  Redeemed out of profits  Redeemed out of proceeds of a fresh issue of shares  Capital reduction — S.256A – S.256E
	Single shareholder company  Multiple shareholder company. A Form 2560 must be lodged before a capital reduction takes place  Share buy-back.—ss.257H(3)
··	Minimum holding buy-back by listed company  Other buy-back type: A form 280 or 281 must be lodged at least 14 days, and no more than 1 year before the share buy-back can take place  Forfeited shares — S 258D
	Shares returned to a public company — ss.258E(2) & (3)  Under section 651C, 724(2), 737 or 738  Under section 1325A (court order)
	Other Description Give section reference
Details of cancelled shares	List the details of shares cancelled in the following table  Share class code Number of shares cancelled Amount paid (cash or otherwise)
	Earliest date of change : Please indicate the earliest date that any of the above changes occurred.

# C2 Issue of shares

	j	- Continue of the last of the						re	
ORD	1,200	) —————		20 C	ends_		Nil		<del></del>
	·			<del></del>				····	
est date of cha									
e indicate the e	arliest date that any of l	the above change	s occurred						
The state of the s	l [Y Y] I for other than cash, w	ere some or all of	the shares issue	ed under a written	contract?				
Yes if yes, propriet	tary companies must a	lso lodge a Form	2072 certifying t	that all stamp dutie	s have been pa	d. Public com	anies must als	o lodge a F	orm 201
and either a F No	orm 208 or a copy of th	e contract.							
	ary companies are not r	equired to provide	e any further doo	cuments with this fo	om. Public com	panies must a	so lodge a Fon	n 208.	
hanga te	o share struct	furo							
Jilanye u									
•			as a result of the	a issue or cancellat	ion of shares), r	olease show th	e uodated detai	ils for the st	hare cla
a change to the d. Details of sha	share structure table hare classes not affected	as occurred (eg. a by the change are							
a change to the d. Details of sha	share structure table h	as occurred (eg. a by the change are			Total numbe	rof Total ent Paid	amount on these	Total amo unpaid or	unt
a change to the d. Details of sha are	share structure table hare classes not affected	as occurred (eg. i by the change and rd	e not required h	ere. Shares	Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt Lihese
a change to the d. Details of sha are ss code	share structure table hare classes not affected Full title if not standa	as occurred (eg. i by the change and rd	e not required h		Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt i these
a change to the d. Details of sha are ss code	share structure table have classes not affected Full title if not standa	as occurred (eg. i by the change and rd	e not required h	ere. Shares	Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt i these
a change to the d. Details of sha are ss code	share structure table have classes not affected Full title if not standa	as occurred (eg. i by the change and rd	e not required h	ere. Shares	Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt i these
a change to the d. Details of sha are ss code	o share structure table have classes not affected  Full title if not standa  ORDINA COPTIONS	as occurred (eg. i by the change and rd	e not required h	ere. Shares	Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt i these
a change to the d. Details of sha are ss code	Share structure table have classes not affected Full title if not standa  OROLLAR COPTIONS  ange earliest date that any of	as occurred (eg. a by the change and a second a second and a second and a second and a second and a second an	e not required h	ere. Shares	Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt i these
a change to the d. Details of sha are ss code  OROMAN Prows  est date of chase indicate the conditions are second and the conditions are indicated the conditions.	Share structure table have classes not affected Full title if not standa  OROLLAR COPTIONS  ange earliest date that any of	as occurred (eg. a by the change and a second a second and a second and a second and a second and a second an	e not required h	ere. Shares	Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt i these
a change to the d. Details of sha are ss code  OROMAN AND THE SE INCIDENTAL SE INDICATE THE SE	Share structure table have classes not affected Full title if not standa  OROLAGO  OPTIONS  ange earliest date that any of	as occurred (eg. a by the change and a second a second and a second and a second and a second and a second an	e not required h	ere. Shares	Total numbe shares (curr after change	r of Total ent paid s) shar 5,25035	amount on these es: ,106,251•5	Total amo unpaid or shares	unt i these

# C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to Please indicate the na of the member whose changed	me and address	Family	y name		iven names			
			any name					
		ACN/ARBN	/ ABN	number				
			per and Street na					
		Suburb/City Postcode		Country (if no	tAustralia)		] State/	Territory.
Earliest date of chan Please indicate the ea of the following chang	rilest date that any	السا لسا ا	nge // // // // // // // [M M] [Y	Y				
The changes are Share class Code		Shares decreased by (number)	Total number now held	"Total \$ paid on these shares	"Total \$ unpaid on these shares	Fully paid. (y/n)	Beneficially held (y/n)	Top 20. member (y/n)
*Public come space	are not required to p	muda haca waa						
Date of entry of mer register (New members only)	mber's name in	Date of en						

# of continued... Further changes to the register of members

- Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

   If there are 20 members or less in a share class, all changes need to be notified

   If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)

   If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to Please indicate the name and address of the member whose shareholding has	Family name:		Given names			
changed	OR Company name					
	ACN/ARBN/ABN					
	Office, unit, level, or PO Box					
·	Suburb/City				] State/1	emtory
Earliest date of change	Postcode  Date of change	Country (if no)	Australia)			
Please indicate the earliest date that any of the following changes occurred.  The changes are	D DI [M M] Y	M				
code Increased by d	Shares Total number decreased by now held (number)	*Total \$ paid on these : shares	*Total \$ unpaid on these shares	Fully paid (y/n)	Beneficially held (y/n)	Top 20. member (y/n)
*Public companies are not required to pro Date of entry of member's name in register	ovide these details.  Date of entry					
(New members only)		Ŋ				



20 July 2004

# Antisense Therapeutics Establishes New Research Laboratory at Murdoch Childrens Research Institute

Antisense Therapeutics Limited (ASX:ANP) has established a new laboratory to support its research into novel antisense drugs for human disease. The laboratory will be located in new research & development facilities at the Murdoch Childrens Research Institute (MCRI), a founding research partner of the Company.

Antisense Therapeutics and MCRI recently concluded their research agreement on the development of a cream therapy for the common skin disorder, psoriasis, marking the successful completion of pre-clinical research on the psoriasis drug ATL1101. The Company has since announced its intention to test ATL1101 in a proof of concept study in patients with psoriasis, with the study on track to commence before the end of this year.

The Antisense Therapeutics laboratory will support the Company's antisense drug research pipeline, which includes drugs targeting major inflammatory diseases, growth abnormalities and vision-related disorders. Antisense Therapeutics manages its animal pharmacology experiments by establishing relationships with contract research organisations, Universities and Institutes throughout the world.

"We work with the leading scientific experts in each new disease area that we target" said Antisense Therapeutics' Research Director, Dr Christopher Wraight. "Our contractors are experts in testing drugs in their animal models for each disease, while our expertise is in applying and testing antisense drugs to that disease. So the antisense-specific aspects of each animal study will be transferred to our laboratory, such as measuring the antisense drug's effects in the tissues of treated animals. We believe this is the most time-efficient and cost-effective way to ensure the quality of our drug testing programme, and it is in keeping with our out-sourced or "virtual" business model."

"We are very pleased to be continuing our relationship with the MCRI, one of Australia's leading medical research institutes" said Antisense Managing Director Mark Diamond. The Antisense Therapeutics laboratory is headed by Dr Lynne Atley, who recently joined the Company following her role as Group Leader at MCRI for the Antisense Therapeutics-MCRI collaborative research programme on ATL1101 for psoriasis.

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101). ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies. ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS) and Queensland Investment Corporation.

The *Murdoch Childrens Research Institute* is a major Australian independent research institute based at the Royal Children's Hospital and affiliated with the University of Melbourne. The MCRI conducts life-saving medical research, combining priority driven public health innovation with new genetic technologies and clinical know-how.

ATL1101 is an antisense drug designed to silence, or suppress, the gene for the insulin-like growth factor-I receptor (IGF-Ir). IGF-Ir's pivotal role in the regulation of cell over-growth in the common skin disorder, psoriasis, was established from work conducted by Antisense Therapeutics' Melbourne collaboration partner, the Murdoch Childrens Research Institute. Psoriasis is a debilitating disease characterised by red, flaking skin lesions. ATL1101 is being developed as a cream treatment for mild-to-moderate cases of psoriasis.

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999



28 July 2004

# **Investor Update**

# Further Market Developments re Treatments for Multiple Sclerosis

On 26 July 2004, competitor company Biogen Idec and its partner Elan Corporation plc, announced "that the US Food and Drug Administration (FDA) has formally accepted their Biologics License Application (BLA) for Antegren® (natalizumab)...Acceptance of a filing indicates that the FDA has determined that the application is complete and permits a substantive review."

Both Antegren® and Antisense Therapeutics' MS compound ATL1102 target the VLA-4 protein (Alpha-4 integrin chain), which is considered to be responsible for the progression of MS. This news by Biogen/Elan provides Antisense Therapeutics with greater confidence in the likely success of ATL1102.

This recent announcement by Biogen/Elan follows an announcement made by them in June 2004 where the companies advised that "the BLA for Antegren® (natalizumab) had been designated for Priority Review and Accelerated Approval by the FDA for the treatment of multiple sclerosis. Antisense Therapeutics released an investor update with respect to this news on 1 July 2004.

As advised by Biogen/Elan, "The FDA grants Priority Review status to products that are considered to be potentially significant therapeutic advancements over existing therapies that address an unmet medical need. Based on the FDA's designation of Priority Review for natalizumab in MS, the companies anticipate action by the Agency approximately six months from the submission date, rather than 10 months for a standard review. On 25 May 2004, the companies (Biogen/Elan) announced they had previously submitted the BLA for the approval of natalizumab for MS."

Both Biogen Idec (market cap: US\$19.2 billion) and Elan (market cap: €6.2 billion) have enjoyed significant increases in their respective share prices on the initial release of their news regarding an early filing of a BLA with the FDA in February 2004 (Biogen's share price has increased by 28 per cent and Elan's by 126 per cent to 27 July 2004).

The relevance of Biogen's/Elan's news for Antisense Therapeutics was described in the Company's 1 July 2004 investor update as follows:

### Positive impact on ATL1102 for multiple sclerosis

So how does this impact on Antisense Therapeutics, and more particularly, the development of its own MS drug, ATL1102?

As stated above, both Antegren® and Antisense Therapeutics' MS compound ATL1102 target the VLA-4 protein, which is considered to be responsible for the progression of MS.

ATL1102 is a second-generation antisense drug designed to act at an earlier stage of the disease process (than Antegren®) by preventing excessive amounts of VLA-4 being produced. ATL1102

may also provide important advantages over Antegren®, in particular the cost of therapy and method of delivery, as well as improved effectiveness.

The recent Antegren® news provides Antisense Therapeutics with greater confidence in the likely success of ATL1102. Also, the submission of the Antegren® application to the FDA will establish a path to regulatory approval for ATL1102 and commercially and scientifically validate the Company's MS drug development strategy.

Antisense Therapeutics, which reported positive results from a Phase I trial of ATL1102 in June 2004, is in the process of preparing an application to conduct a Phase IIa clinical trial of this compound in MS patients. Regulatory agency approval and commencement of the Phase IIa trial are expected to occur during the second half of this year.

It is the Company's understanding that, with the exception of Antegren®, there are no other drugs that specifically target VLA-4 in clinical trials in patients with MS. Antisense Therapeutics has a worldwide exclusive license to ATL1102 from Isis. Isis has US granted patents and other pending patent rights over antisense drugs targeting VLA-4. Non-antisense methods of regulating VLA-4 activity are believed to infringe Elan's US patent over Antegren® licensed exclusively to Biogen. This should reduce the likelihood that Antisense Therapeutics and Elan/Biogen Idec will be joined by other competitors with MS treatments targeting VLA-4.

#### About Antisense Therapeutics Limited

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS) and Queensland Investment Corporation.

Contact Information: Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999 2004 NOV 16 P 12: 23

OFFICE OF INTERNATION CORPORATE FROM 100

Rule 4.7B

# Appendix 4C

# Quarterly report for entities admitted on the basis of commitments

Introduced 31/3/2000. Amended 30/9/2001

Name of entity	IMPD
ANTISENSE THERAPEUTICS LIM	HED
ABN	Quarter ended ("current quarter")
41 095 060 745	30 JUNE 2004

# Consolidated statement of cash flows

Cash flows related to operating activities			Current quarter \$A'000	Year to date (12 months) \$A'000
1.1	Receipts from c	ustomers	(38)	842
1.2	Payments for	<ul> <li>(a) staff costs</li> <li>(b) advertising and marketing</li> <li>(c) research and development</li> <li>(d) leased assets</li> <li>(e) other working capital *</li> </ul>	(240) - (443) - (183)	(1,271) (2,278) (538)
1.3 1.4 1.5 1.6 1.7	received Interest and oth Income taxes pa	other items of a similar nature er costs of finance paid aid details if material)	- 186 - -	372
	Net operating	cash flows	(718)	(2,209)

 $<sup>\</sup>mbox{^*}$  Includes GST paid to suppliers and GST credits received from ATO.

<sup>+</sup> See chapter 19 for defined terms.

		Current quarter \$A'000	Year to date (12 months) \$A'000
1.8	Net operating cash flows (carried forward)	(718)	(2,209)
	Cash flows related to investing activities		,
1.9	Payment for acquisition of:  (a) businesses (item 5)		-
	(b) equity investments	- 1	-
	(c) intellectual property	-	-
	(d) physical non-current assets	(8)	(18)
	(e) other non-current assets	-	-
1.10	Proceeds from disposal of:		
	(a) businesses (item 5)		-
	(b) equity investments	-	-
	(c) intellectual	-	•
	property (d) physical non-	1	-
	current assets		-
	(e) other non-current assets	-	•
1.11	Loans to other entities		-
1.12	Loans repaid by other entities	-	-
1.13	Other (provide details if material)	-	•
	Net investing cash flows	(8)	(18)
1.14	Total operating and investing cash flows	(726)	(2,227)
1.15	Cash flows related to financing activities Proceeds from issues of shares, options, etc.		10,397
1.16	Proceeds from sale of forfeited shares		
1.17	Proceeds from borrowings		
1.18	Repayment of borrowings		
1.19	Dividends paid		(204)
1.20	Other - costs relating to issue of shares		(294) 10,103
	Net financing cash flows		
	Net increase (decrease) in cash held	(726)	7,875
1.21	Cash at beginning of quarter/year to date	15,147	6,546
1.22	Exchange rate adjustments to item 1.20	•	-
1.23	Cash at end of quarter	14,421	14,421

<sup>+</sup> See chapter 19 for defined terms.

# Payments to directors of the entity and associates of the directors Payments to related entities of the entity and associates of the related entities

		Current quarter \$A'000	
1.24	Aggregate amount of payments to the parties included in item 1.2		76
1.25	Aggregate amount of loans to the parties included in item 1.11		-

1.26 Explanation necessary for an understanding of the transactions

Item 1.24 Reflects the following related party payments:

- (a) Total amounts paid to directors include director's fees, salaries and superannuation of \$75,531 (YTD: \$417,585).
- (b) Dr Stanley Crooke, a director of the Company is also a director of Isis Pharmaceuticals Inc ("Isis"). A total amount of \$79,590 (YTD: \$278,740) was paid to Isis for research and development related services provided by them to Antisense Therapeutics Limited ("ATL").
- (c) Professor George Werther, a director of the company, is an executive officer of the Murdoch Childrens Research Institute ("MCRI"). An amount of \$Nil (YTD: \$334,240) was paid to the MCRI for research services performed by them for ATL.
- (d) Dr Chris Belyea, a director of the company, is the Managing Director of Metabolic Pharmaceuticals. An amount of \$1,602 was paid to Metabolic Pharmaceuticals as reimbursement of expenses made on behalf of ATL (YTD: \$2,219.33).

# Non-cash financing and investing activities

2.1	Details of financing	and investing	transactions	which	have	had a	material	effect	on	consolidated
	assets and liabilities l	but did not inve	olve cash flow	ws.						

assets and natiffices but aid not involve	cusii iiows	
Not applicable.		-

2.2 Details of outlays made by other entities to establish or increase their share in businesses in which the reporting entity has an interest

Not applicable.		-

### Financing facilities available

Add notes as necessary for an understanding of the position. (See AASB 1026 paragraph 12.2).

3.1 Loan facilities

Amount available	Amount used
\$A'000	\$A'000
-	-

<sup>+</sup> See chapter 19 for defined terms.

# Appendix 4C Quarterly report for entities admitted on the basis of commitments

3.2	Credit standby arrangements	-	-

<sup>+</sup> See chapter 19 for defined terms.

# Reconciliation of cash

show	nciliation of cash at the end of the quarter (as in the consolidated statement of cash flows) to elated items in the accounts is as follows.	Current quarter \$A'000	Previous quarter \$A'000
4.1	Cash on hand and at bank	3,921	2,647
4.2	Deposits at call	10,500	12,500
4.3	Bank overdraft	-	-
4.4	Other (provide details)	-	-
	Total: cash at end of quarter (item 1.23)	14,421	15,147

# Acquisitions and disposals of business entities

		Acquisitions (Item 1.9(a))	Disposals (Item 1.10(a))	
5.1	Name of entity	Not applicable	Not applicable	
5.2	Place of incorporation or registration			
5.3	Consideration for acquisition or disposal			
5.4	Total net assets			
5.5	Nature of business			

# Compliance statement

- 1 This statement has been prepared under accounting policies which comply with accounting standards as defined in the Corporations Act (except to the extent that information is not required because of note 2) or other standards acceptable to ASX.
- 2 This statement does give a true and fair view of the matters disclosed.

Sign here:

Date:

30 July 2004

Print name:

Mark Diamond

<sup>+</sup> See chapter 19 for defined terms.

# Notes

- 1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity wanting to disclose additional information is encouraged to do so, in a note or notes attached to this report.
- 2. The definitions in, and provisions of, AASB 1026: Statement of Cash Flows apply to this report except for the paragraphs of the Standard set out below.
  - 6.2 reconciliation of cash flows arising from operating activities to operating profit or loss
  - 9.2 itemised disclosure relating to acquisitions
  - 9.4 itemised disclosure relating to disposals
  - 12.1(a) policy for classification of cash items
  - 12.3 disclosure of restrictions on use of cash
  - 13.1 comparative information
- 3. Accounting Standards. ASX will accept, for example, the use of International Accounting Standards for foreign entities. If the standards used do not address a topic, the Australian standard on that topic (if any) must be complied with.

<sup>+</sup> See chapter 19 for defined terms.

RECEIVED	
2001 NOV 16 P 12: 23	Form 484
Strian -	Corporations Act 2001

# Change to company details

Sections A, B or C may be lodged independently with this signed cover page to notify ASIC of:

- A1 Change of address
- A2 Change of name officeholders or members
- A3 Change ultimate holding company
- B1 Cease company officeholder
- B2 Appoint company officeholder
- B3 Special purpose company

- C1 Cancellation of shares
- C2 Issue of shares
- C3 Change to share structure
- C4 Changes to the register of members

Company details	Company name	r de la la companya de la la la companya de la comp
, •	ANTISCUSE THERAPENTIC	S LIMITED
lefer to guide for information about	ACN/ABN	Corporate key
orporate key	41 095 060 745	788 41 339
odgement details	Who should ASIC contact if there is a query about this	form?
	NATALIE KORLITEV	
	ASIC registered agent number (if applicable)	
•	Telephone number	
	(03) 98278999	
	Postal address	
	LEVELI, 10 WALLALE	Avenue Toonar.
	VIC. 3142	
	Total number of pages including this cover sheet Ple	ase provide an estimate of the time taken to complete this fo
		hrsmins
<u>,</u>		
Signature	off-ook older of the company	
This form must be signed by a current o	Talka Maria Alaka Maria Maria Andrea a Angala A	
	<ul> <li>Lertify that the information in this cover sheet and the att.</li> <li>Name</li> </ul>	ached sections of this form are true and complete.
	NATALLE KORGAN	
	Capacity	
	Director	
	Company secretary	
	Signature	
	N. Korchev	
	Date signed	
	260804	
i		
Lodgement	Send completed and signed forms to:	For help or more information
	Australian Securities and Investments Commission,	Telephone 03 5177 3988

PO Box 4000, Gippsland Mail Centre VIC 3841.

Or lodge the form electronically by visiting the ASIC website

Email info.enquiries@asic.gov.au

Web www.asic.gov.au

www.asic.gov.au

# Section C completion guide

# Standard share codes

Refer to the following table for the share class codes for sections C1, C2, C3 and C4

		Share class code	Full title
A	A	PRF	preference
B	Betc	CUMP	cumulative preference
EMP	employee's	: NCP	non-cumulative preference
FOU	founder's	REDP	redeemable preference
LG	life governor's	NRP	non-redeemable preference
MAN	management	CRP	
ORD	ordinary.	NGRP	cumulative redeemable preference
RED	redeemable	PARP	non-cumulative redeemable preference
SPE	special	I FALL	participative preference

If you are not using the standard share class code, enter a code of no more than 4 letters and then show the full title

Sections to complete

Use the table below to identify the sections of this form to complete (please indicate the sections that have been completed). Completion of this table is optional.

	C1 - Cancellation of shares	C2 • Issue of shares	C3 - Change to share structure table	C4 Change to members register
Issue of shares				
Propnetary company	Not required	1/		
Public company				
f in response to the Annual company statement	Not required	<b>/</b>	/	1
if not in response to the Annual company statement	Not required		Not required	Not required
Cancellation of shares				
Proprietary company	/	Not required		7
Public company  f in response to the Annual				
Company statement		Not required	1	7
If not in response to the Annual company statement		Not required	Not required	Not required
Transfer of shares		14-14-150		
Proprietary company	Not required	Nat required	Not required	1
Public company  If in response to the Annual	1122			
company stafement	Not required	Not required	Not required	<b>/</b>
If not in response to the Annual company statement	Not required	Not required:	Not required	Not required
Changes to amounts paid Proprietary company				
- Rublic company	Not required	Not required	1	1
if in response to the Annual	Not required	Not required		
company statement			<b>/</b>	✓
if not in response to the Annual company statement	Not required	Nat required	Not required	Not required
Changes to beneficial ownership  Proprietary company	Not required	No.		
Public company	iver redoited	Not required	Not required ::	<b>V</b>
if in response to the Annual	Not required	Nat required	Votroguess	
company statement if not in response to the Annual company statement	Not required	Not required	Not required	<b>/</b>

To notify ASIC about a division or conversion of a class of shares, you must lodge a form 211 within 28 days of the change occurring.

To notify ASIC about a conversion of shares into larger or smaller numbers, you must lodge a form 2205B within 28 days of the change occurring.

# C1 Cancellation of shares

leason for cancellation	Redeemable preference shares — S.254J	
Please indicate the reason that shares ave been cancelled (select one or more	Redeemed out of profits	
oxes)	Redeemed but of proceeds of a fresh issue of shares	
	Capital reduction — S.256A – S.256E	
	Single shareholder company	
	Multiple shareholder company. A Form 2560 must be lodged before a capital reduction takes	s place
	Share buy-back — ss.257H(3)	
•	Minimum holding buy-back by listed company	
	Other buy-back type. A form 280 or 281 must be lodged at feast 14 days, and no more than share buy-back can take place	1 year before the
	Forfeited shares — \$.258D	
	F—Shares returned to a public company — ss.258E(2) & (3)	
	Under section 651C, 724(2), 737 or 738	
	Under section 1325A (court order)	
•	Other	
	<u>Description</u>	
	Give section reference	
Details of cancelled shares	List the details of shares cancelled in the following table	
	Share class code Number of shares cancelled Amount paid (cash or otherwise)	
		-
		-
		-
,	Earliest date of change Please indicate the earliest date that any of the above changes occurred.	
	[D D] [M M] [Y Y]	

ASIC Form 484 26 February 2004 Section C Page 2 of 5

# C2 Issue of shares

List details of new share issues in the following table.

ord		I						
	5,000		20 ce	nts	-	Nil.		
				<del></del>		··		
···	<del> </del>							
·	<u> </u>			41 Y.P	<del></del>			
est date of cha	Inge							
se indicate the e	earliest date that any of th	ne above changes occurre	d					7
[],O[8 : D]: [M								
ares were issue	Charles and the second of the	re some or all of the share	es issued under a wr	iten contract?				W
Yes if yes, proprie	etary companies (must als	so lodge a Form 207Z cert	tifying that all stamo	duties have been paid	I. Public como	anies müst als	o lodge a Form	201
and either a F	Førm 208 or a copy of the	eontract						
No - t no propriet	ary companies are not re	equired to provide any furth	aar documents with	his form Public com	anios mustale	a ladaa a For	n 208	
			ici documento mu		idilles filusi ak	onlooge a ribii	1,720	
Change t	o share struct	ure					······································	
a change to the	e share structure table ha	as occurred (eg. as a resul	It of the issue or can	cellation of shares), pl	ease show the	updated detai	ils for the share	da
ed. Details of sha nare	are classes not affected b Full title if not standar	by the change are not requ	uired here. Dalamentualiscentes	Total number		amount	Total amount	
ass code	ISONOLO IL SUBILIO	<b>4.</b>		shares (curre	nt paid o	n these	unpaid on thes	se
)RO	O O . May	-	Cuases	after changes			shares っ ろ といし	
SHOUS	Derays Da	on onouny	Simace	355,258, 125,412	1 1	٠ ١		
1100	101125000	st decision	DIMM25	143,412	۱ <u>۵۶ (۱۵۵ )</u>	, 13 (1-13)	7010	<u> </u>
	<del>                                     </del>							
	ange							
tiest date of ch		the above changes occur	ed					
at Planter Line and Burner Steel Steel								
ase indicate the	NJ Y YJ	/ Welly /						w.
ase indicate the D) [M N	M (Y Y) B (O (4) N (4)	(orchal						

ASIC Form 484 26 February 2004 Section C Page 3 of 5

# C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to Please indicate the name and address of the member whose shareholding has		Famil	y name		Siven names			
hanged	anarenowny nas	OR Gome	Dany name					
		ACN/ARBN						
			level, or PO Box					
		Street num Suburb/City	per and Street na	me.				
		Postcode		Country (if no	t Australia)		State/fu	emiory
Earliest date of char Please indicate the e of the following chan	arliest date that any	Date of charge of the charge o						
The changes are Share class code	increased by	Sharesdecreased by(rumber)	Total number now held	*Total \$ paid on these shares	"Total \$ unpaid on these shares	Fully paid (y/n)	Beneficially field (y/n)	Top 20 member (y/n)
*Public companies	s are not required to p	rovide these detail	S					
Date of entry of me register (New members only)		Date of en	try. , , , , , , , , , , , , , , , , , , ,					

# C4 Continued... Further changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

The changes apply to Please indicate the name and addres of the member whose shareholding h		name	G	yen names			
changed	OR Comp	any name					
	ACN/ARBN/				######################################		
		level, or PO Box n					
	Suburb/City					State/	Territory
	Postcode		Country (if not	Australia)			
Earliest date of change Please indicate the earliest date tha of the following changes occurred.		nge // // // // // // // // // // // // //	Ŋ				
The changes are Share class Shares code increased by	Shares decreased by (number)	Total number now held	*Total \$ paid on these shares	*Total \$ unpaid on these shares	Fully paid (y/n)	Beneficially held (y/n)	Top 20 member (y/n)
*Public companies are not required  Date of entry of member's name register							

# MM MOY IS DIP: 97

OFFICE OF INTERNATION OF CORPORATE FIRM

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

# Appendix 3B

# New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002, 1/1/2003.

Name	of entity	
ANT	ISENSE THERAPEUTICS LIMITE	ED
ABN 41 09	95 060 745	
We (	the entity) give ASX the following i	information.
	t 1 - All issues ust complete the relevant sections (attach sh	heets if there is not enough space).
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	Ordinary Shares
2	Number of *securities issued or to be issued (if known) or maximum number which may be issued	3,000
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	Exercise of 3,000 ANPO options at 20 cents each to purchase 3,000 ordinary shares in ANP.

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	Yes	
	If the additional securities do not rank equally, please state:  • the date from which they do  • the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  • the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
5	Issue price or consideration	20 cents per share.	
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	Exercise of 3,000 ANF 3,000 ordinary shares in	
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	11 August 2004	
8	Number and *class of all *securities quoted on ASX (including the securities in clause 2 if applicable)	Number 355,258,250 91,462,865	+Class Ordinary shares (ANP) Options (ANPO)

Appendix 3B Page 2

<sup>+</sup> See chapter 19 for defined terms.

Number +Class Number and +class of all 11,500,000 Options expiring 31 July +securities not quoted on ASX 2005 exercisable at 20 cents (including the securities in clause each (ANPAM) 2 if applicable) 20,000,000 Options expiring 30 November 2006 exercisable at 20 cents each (ANPAO). Options expiring 31 July 2,450,000 2005 exercisable at 20 cents each (ANPAQ) 10 Dividend policy (in the case of a N/A trust, distribution policy) on the increased capital (interests)

# Part 2 - Bonus issue or pro rata issue

11	Is security holder approval N/A required?	
12	Is the issue renounceable or non-renounceable?	
13	Ratio in which the *securities will N/A be offered	
14	<sup>+</sup> Class of <sup>+</sup> securities to which the offer relates N/A	
15	<sup>+</sup> Record date to determine N/A entitlements	
16	Will holdings on different registers (or subregisters) be aggregated for calculating entitlements?	
17	Policy for deciding entitlements in relation to fractions	
18	Names of countries in which the entity has *security holders who will not be sent new issue	
	documents	
	Note: Security holders must be told how their entitlements are to be dealt with.	
	Cross reference: rule 7.7.	
19	Closing date for receipt of N/A acceptances or renunciations	

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a	N/A

Appendix 3B Page 4

<sup>+</sup> See chapter 19 for defined terms.

32	How do *security holders dispose of their entitlements (except by sale through a broker)?	N/A
33	<sup>+</sup> Despatch date	N/A
	t 3 - Quotation of secur	
34	Type of securities (tick one)	
(a)	Securities described in Part 1	
(b)		of the escrowed period, partly paid securities that become fully paid, employee ends, securities issued on expiry or conversion of convertible securities
Enti	ties that have ticked box 34(a	a)
Addi	tional securities forming a new cla	ass of securities
Tick to docum	o indicate you are providing the informa ents	tion or
35		r securities, the names of the 20 largest holders of the number and percentage of additional *securities held by
36	†securities setting out the nun	ry securities, a distribution schedule of the additional aber of holders in the categories
	1 - 1,000 1,001 - 5,000 5,001 - 10,000	
	10,001 - 100,000 100,001 and over	
37	A copy of any trust deed for t	he additional *securities
+ See	chapter 19 for defined terms.	

# Entities that have ticked box 34(b) Number of securities for which N/A <sup>+</sup>quotation is sought 39 Class of \*securities for which N/A quotation is sought 40 Do the \*securities rank equally in all N/A respects from the date of allotment with an existing +class of quoted \*securities? If the additional securities do not rank equally, please state: • the date from which they do the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment 41 Reason for request for quotation N/A Example: In the case of restricted securities, end of restriction period (if issued upon conversion of another security, clearly identify that other security) Number +Class Number and <sup>+</sup>class of all <sup>+</sup>securities N/A N/A quoted on ASX (including the

securities in clause 38)

Appendix 3B Page 6

<sup>+</sup> See chapter 19 for defined terms.

#### Quotation agreement

- <sup>†</sup>Quotation of our additional <sup>†</sup>securities is in ASX's absolute discretion. ASX may quote the <sup>†</sup>securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will
    not require disclosure under section 707(3) or section 1012C(6) of the
    Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before †quotation of the †securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here:

Natalie Korchev

Date: 26 August 2004

Company secretary

Print name:

Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.





26 August 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Total number of pages: 39

Dear Sir/Madam

Re: PRELIMINARY FINAL REPORT (APPENDIX 4E) (AUDITED) FINANCIAL YEAR ENDED 30 JUNE 2004

In accordance with Listing Rule 4.3A we enclose the Preliminary Final Report (Appendix 4E) (audited) on the results of Antisense Therapeutics Limited ('Antisense Therapeutics' or 'the company') for the year ended 30 June 2004.

#### Results

The Directors report a loss after income tax for the period of \$4,609,624 (2003: \$6,107,898) which includes an income tax benefit of \$371,820 (2003: \$nil). The loss is after fully expensing all research and development costs.

The receipt of payments under the R&D Start Grant awarded to the psoriasis project (\$692,375) and the cash rebate received in relation to the Research and Development Tax Concession (\$371,820) have contributed to the reduction in the loss this year compared to the previous financial year. The Operations Report provides further details regarding the progress made by the company over the period, which have contributed to its result for the year.

During the period, the company raised \$10.4 million through new share issues.

Antisense Therapeutics has no borrowings and has cash and bank term deposits as at 26 August 2004 amounting to \$13.2 million.

#### Key Highlights

The company reported substantial progress in its Research and Development activities over the period under review with a focus on meeting the key project milestones for its lead compounds, ATL1102 and ATL1101. Major achievements included:

### Multiple Sclerosis (ATL1102) Project

On 8 June 2004, the Company announced positive results following the completion of the Phase I human clinical trial for ATL1102. Fifty-four healthy volunteers participated in the double-blind, dose-escalation, placebo-controlled, randomized study, which evaluated the pharmacokinetic and safety profile of ATL1102. The Company is now in the process of preparing an application to conduct a Phase IIA clinical trial in MS patients.

# Psoriasis (ATL1101) Project

In July 2003, the Company announced its plans to undertake a "proof-of-concept" study in patients with Psoriasis. Since that time the manufacture of the bulk active pharmaceutical ingredient (API) and formulation of injectable and cream formulations of ATL1101 has been completed. Pre-clinical animal toxicology studies to support this study are currently underway.

### Growth & Sight Disorders (ATL1103) Project

In February 2004 the Company announced that an antisense inhibitor designed to block the Growth Hormone receptor (GHr) gene had produced definitive results in an experimental system in mice confirming its potential as a treatment for growth and sight disorders. Based on these animal studies the Company has confirmed its intention to move this compound into development.

#### Other Projects

In addition to progressing its most advanced projects through pre-clinical and clinical development, during the year the Company conducted animal studies on a number of new research compounds. The identification and testing of potential new antisense compounds is integral to the development of the Company's drug pipeline.

Further details regarding the progress of the company's operations are provided in the Operations Report included in the Appendix 4E attached.

This letter and the attached Appendix 4E Preliminary Final Report form part of this announcement to the Australian Stock Exchange Limited.

Yours faithfully

Antisense Therapeutics Limited

Mark Diamond Managing Director

# **APPENDIX 4E**

# **Preliminary Final Report**

Name of entity:

ANTISENSE THERAPEUTICS LIMITED

ABN:

41 095 060 745

Reporting period:

FINANCIAL YEAR ENDED 30 JUNE 2004

Previous

Corresponding period: FINANCIAL YEAR ENDED 30 JUNE 2003

# **INDEX**

- 1. Results for announcement to the market
- 2. Commentary on Results
- 3. Operations Report
- 4. Financial Report
- 5. Other Information

**Note:** The financial figures provided are in <u>actual</u> Australian dollars, unless specified otherwise.

# RESULTS FOR ANNOUNCEMENT TO THE MARKET

The results of Antisense Therapeutics Limited for the year ended 30 June 2004 are as follows:

Revenues and Results from Ordinary Activities:		Change compared to 2003	2004 \$	
Revenues from ordinary activities	Up by \$893,311	199%	1,341,377	
Profit (loss) from ordinary activities after tax attributable to members	Loss has decreased by \$1,498,274	25%	(4,609,624)	
Net profit (loss) for the period attributable to members	Loss has decreased by \$1,498,274	25%	(4,609,624)	

#### Dividends:

No dividends have been paid or declared by the entity since the beginning of the current reporting period.

No dividends were paid for the previous corresponding period.

# Brief Explanation of figures reported above:

Revenue from ordinary activities increased in the current period due to increased interest income and the receipt of payments under the R&D Start Grant awarded to the psoriasis project. The loss for the company for the year was \$4,609,624 (2003: \$6,107,898) including an income tax benefit of \$371,820 (2003: \$nil). The loss is after fully expensing all research and development costs. The receipt of payments under the R&D Start Grant awarded to the psoriasis project (\$692,375) and the cash rebate received in relation to the Research and Development Tax Concession (\$371,820) have contributed to the reduction in the loss this year compared to the previous financial year.

For further details relating to the current period's results, refer to the "Commentary on Results" on the following page.

#### **COMMENTARY ON RESULTS**

(As communicated in the cover letter to this Appendix 4E)

The Directors report a loss after income tax for the period of \$4,609,624 (2003: \$6,107,898) which includes an income tax benefit of \$371,820 (2003: \$nil). The loss is after fully expensing all research and development costs.

The receipt of payments under the R&D Start Grant awarded to the psoriasis project (\$692,375) and the cash rebate received in relation to the Research and Development Tax Concession (\$371,820) have contributed to the reduction in the loss this year compared to the previous financial year. The Operations Report provides further details regarding the progress made by the company over the period, which have contributed to its result for the year.

During the period, the company raised \$10.4 million through new share issues.

Antisense Therapeutics has no borrowings and has cash and bank term deposits as at 26 August 2004 amounting to \$13.2 million.

#### **Key Highlights**

The company reported substantial progress in its Research and Development activities over the period under review with a focus on meeting the key project milestones for its lead compounds, ATL1102 and ATL1101. Major achievements included:

#### Multiple Sclerosis (ATL1102) Project

On 8 June 2004, the Company announced positive results following the completion of the Phase I human clinical trial for ATL1102. Fifty-four healthy volunteers participated in the double-blind, dose-escalation, placebo-controlled, randomized study, which evaluated the pharmacokinetic and safety profile of ATL1102. The Company is now in the process of preparing an application to conduct a Phase IIA clinical trial in MS patients.

#### Psoriasis (ATL1101) Project

In July 2003, the Company announced its plans to undertake a "proof-of-concept" study in patients with Psoriasis. Since that time the manufacture of the bulk active pharmaceutical ingredient (API) and formulation of injectable and cream formulations of ATL1101 has been completed. Pre-clinical animal toxicology studies to support this study are currently underway.

## Growth & Sight Disorders (ATL1103) Project

In February 2004 the Company announced that an antisense inhibitor designed to block the Growth Hormone receptor (GHr) gene had produced definitive results in an experimental system in mice confirming its potential as a treatment for growth and sight disorders. Based on these animal studies the Company has confirmed its intention to move this compound into development.

# Other Projects

In addition to progressing its most advanced projects through pre-clinical and clinical development, during the year the Company conducted animal studies on a number of new research compounds. The identification and testing of potential new antisense compounds is integral to the development of the Company's drug pipeline.

Further details regarding the progress of the company's operations are provided in the Operations Report which follows.

# **Operations Report**

# Overview of Company's Activities

The company has made substantial progress in its Research and Development activities since the last financial year with a focus on meeting the key project milestones for its lead compounds, ATL1102 and ATL1101 and the addition of a new project to the drug development pipeline. The key achievements announced by the company were:

- ATL1102 for Multiple Sclerosis successful completion of the Phase I human clinical trial
- ATL1101 for Psoriasis in July 2003 the company announced its plans to underake a "proof-of-concept" study in patients with Psoriasis. Since that time the manufacture of injectable and cream formulations of ATL1101 has been completed and the pre-clinical animal toxicology studies to support this study have commenced.
- ATL1103 for Growth and Sight Disorders the successful testing in animals of a new antisense
  compound designed to block Growth Hormone receptor (GHr) expression confirmed its potential
  as a treatment for growth and sight disorders. The company intends moving this compound into
  development.
- During the period the company successfully raised \$10.4 million in a private placement of shares to Australian institutions and professional investors and through the issue of shares to eligible shareholders pursuant to the company's Share Purchase Plan.

## Antisense Therapeutics' Mission

Antisense Therapeutics' mission is to create, develop and commercialise novel antisense pharmaceuticals. The company's primary focus is to progress its two lead compounds (ATL1102 and ATL1101) through research and clinical trials with the aim of providing new and improved therapies for the treatment of Multiple Sclerosis and Psoriasis respectively, and to support these lead compounds by building a pipeline of additional antisense therapeutics

### Antisense Technology - How It Works

Proteins play a central role in virtually every aspect of human biology. Each of our genes is a set of instructions for the manufacture inside the cell of a particular unique protein. Conventional pharmaceutical drugs typically bring about their desired therapeutic effect by binding to a target protein directly, to interfere with its action.

Antisense drugs are synthetic RNA-like and DNA-like compounds designed for use as medicines, which block disease processes by targeting messenger RNA with extraordinary precision. Unlike conventional small-molecule medicines, the discovery of which requires time-consuming and laborious trial-and-error, antisense medicines are rationally designed by directly exploiting the huge body of genetic information now available from the human genome project. Compared to conventional drugs antisense aims to provide faster, more predictable drug discovery, with increased specificity of action and uniformity of methods of manufacture, formulation and delivery.

Antisense drugs have the potential to treat a wide range of conditions and diseases including autoimmune, infectious, inflammatory, dermatological, metabolic and cardiovascular diseases as well as cancer. There are currently over 20 antisense drugs in clinical trials worldwide to treat various diseases, with more than half of these in Phase II or later stage clinical development. There is already one antisense drug approved for clinical use, and it is anticipated that several more will enter the market over the next few years.

# **Overall Operating Strategy**

Antisense Therapeutics' strategy is:

- to gain access to the best enabling antisense technologies through partnership with key antisense technology leaders;
- to create candidate antisense drugs for diseases where there are large and/or poorly met markets, in collaboration with Antisense Therapeutics' technology and research partners;
- to out-source pre-clinical and clinical testing of the candidate drugs to expert contractors; and
- to commercialise the drugs that are shown to be successful through licensing deals or other partnerships with major pharmaceutical companies.

The company's "virtual structure" minimises infrastructure and overhead costs. This is achieved by working with contractors and consultants on a worldwide basis in order to gain access to the best possible expertise in each area of the company's development operations. These outsourcing activities are closely controlled by the company's management, which has extensive experience in the research and clinical development of pharmaceutical products.

A key aspect to the company's out-sourcing strategy is the collaborations it has developed with Isis Pharmaceuticals Inc ("Isis") and the Murdoch Childrens Research Institute ("MCRI"). The company has made substantial technical progress with its developments over the period under review due to the commitment and expertise of its collaboration partners.

## Isis Strategic Partnership

A fundamental element of the Antisense Therapeutics strategy is its access to state of the art antisense technology, both in respect of know-how and intellectual property to accelerate drug discovery and development. As the leader in the antisense field, Isis is the ideal technology partner for Antisense Therapeutics. Isis currently has one antisense drug on the market (VitraveneTM) and 10 antisense products in development. Isis has several partnerships with major pharmaceutical companies.

The collaboration agreement with Isis provides Antisense Therapeutics with access to Isis's antisense drug discovery technology to commercialise antisense drugs to a number of protein targets including IGF-1R for Psoriasis and an exclusive license to ATL1102, which Antisense Therapeutics is currently progressing through clinical development for Multiple Sclerosis. Isis has large scale antisense manufacturing capabilities and significant manufacturing capacity, and has already manufactured batches of bulk drug product for Antisense Therapeutics and will be available to manufacture further quantities for use in clinical trials.

The collaboration agreement with Isis also provides access to and assistance in expanding Antisense Therapeutics' drug pipeline including the rapid generation of antisense lead compounds to potential therapeutic targets.

#### MCRI Strategic Collaboration

The MCRI, based at the Royal Children's Hospital in Melbourne is a major Australian research institute and operates as an independent non-profit organisation.

Antisense Therapeutics has entered into agreements with the MCRI by which it has obtained the exclusive worldwide rights to commercialise antisense drugs for Psoriasis and other skin diseases. As part of its research agreement with Antisense Therapeutics, the MCRI provides scientific support of the pre-clinical and clinical development, including laboratory testing of the Isis-generated drugs and formulations.

# **Projects Update**

**Multiple Sclerosis: ATL1102** 

#### Background

Multiple Sclerosis (MS) is a life-long, chronic, incurable disease, which progressively destroys the central nervous system (CNS). It is commonly diagnosed between the ages of 20 and 40 years. According to the National Multiple Sclerosis Society, MS is an autoimmune disease that affects the CNS. Approximately 400,000 Americans acknowledge having MS, and every week about 200 individuals are diagnosed. Worldwide, MS may affect more than two million people.

The development of improved Multiple Sclerosis medications is a high opportunity area. There is no cure for MS – the goals of therapy are to improve recovery from attacks, to prevent or lessen the number of relapses and their severity, and to reduce disease progression. Until recently steroids were the principal medications for MS – while steroids cannot affect the progression of MS, they can reduce the duration of attacks. Interferon beta drugs appeared on the market in the early 1990's, however while they have proved an undoubted commercial success, they have significant short comings including poor tolerability and response rates in some patients, in addition efficacy appears to diminish over time.

ATL1102 is a second-generation antisense inhibitor of CD49d, a sub-unit of VLA-4 (Very Late Antegen-4). In MS, white blood cells (leukocytes) are believed to inappropriately migrate from the blood into the CNS. The inhibition of VLA-4 may prevent white blood cells from entering the CNS to stop the progression of MS. ATL1102 is designed to block the over production of VLA-4.

Clinical evidence for VLA-4 target activity in patients with MS has been demonstrated by the successful Phase II clinical studies undertaken on the monoclonal antibody drug, Antegren®, being developed by competitor company, Biogen Idec and its partner Elan Corporation plc. Both Antegren® and ATL1102 target VLA-4, which, as described above, is considered to be responsible for the progression of MS, however, ATL1102 may provide advantages over Antegren® in regards to cost of therapy, method of delivery and improved effectiveness.

#### **Progress**

In August 2003, Antisense Therapeutics commenced Phase I human clinical trials of ATL1102 at the Charterhouse Clinical Research Unit of the Ravenscourt Park Hospital (formerly Stamford Hospital) in London. The aims of these Phase I trials were to obtain information on the pharmacokinetic behaviour of ATL1102 in humans and to assess the safety and tolerability of increasing does levels of ATL1102 injected as single and multiple doses. Fifty-four healthy volunteers participated in the double-blind, dose-escalation, placebo-controlled, randomized study. ATL1102 was either delivered in an intravenous (IV) or subcutaneous (SQ) formulation.

Some preliminary data from these clinical trials were presented at the Australian Neuroscience Scientific Conference in Melbourne on 30 January 2004. The Company reported at this time that preliminary indications from the data collected and analysed were favourable for both safety and pharmacokinetics.

Antisense Therapeutics announced final results from these trials in June 2004. Based on the study's results, 6mg/kg/week of ATL1102 appeared well tolerated and has been selected as the proposed dose for Phase II development. The most frequently reported side effects included mild "flu-like" symptoms and occasional injection site reactions, which were generally mild and increased in incidence and severity with escalating dose levels, particularly at 12 and 18 mg/kg/week.

In July 2004, Biogen Idec and its partner Elan Corporation plc announced the formal acceptance of their Biologics License Application (BLA) for Antegren® by the US Food and Drug Administration (FDA). The FDA's review of Biogen/Elan's BLA "will be based on one-year data from two ongoing Phase III studies". As stated above in the section headed "Background", both Antegren® and ATL1102 target VLA-4, which is considered to be responsible for the progression of MS. This news provides Antisense Therapeutics with greater confidence in the likely success of ATL1102. Also, the submission of the

Antegren® application to the FDA establishes a path to regulatory approval for ATL1102 and commercially and scientifically validates Antisense Therapeutic's MS drug development strategy.

#### Outlook

Antisense Therapeutics is in the process of preparing an application to conduct a Phase IIA clinical trial in MS patients. The trial is expected to be conducted in Europe and the clinical trial application will be filed with an appropriate European regulatory authority. Regulatory agency approval and commencement of the Phase IIA trial are expected to occur during the second half of 2004.

Psoriasis: ATL1101

#### Background

Psoriasis is a chronic non-contagious skin disorder, which affects around 2% of the population. While the precise cause of Psoriasis is unknown, it is thought to be triggered by an immune system defect leading to excessive skin cell division. When severe, 15-20% of the person's body may be affected. The white scales that usually cover the lesion are composed of dead skin cells, and the redness of the lesion is caused by increased blood supply to the area of rapidly dividing skin cells. Severity varies, with 75% of psoriasis cases classified as "mild to moderate", with the remainder "moderate to severe".

The worldwide market for Psoriasis treatments was valued at US\$500 million in 2002 and there is an acknowledged unmet medical need for more effective and safer treatments. The market is forecast to grow beyond US\$2 billion by 2007 ("Frost & Sullivan") with the emergence of new effective treatments.

In the absence of a cure, the goal for a Psoriasis treatment is to reduce inflammation and/or to slow down rapid skin cell division to decrease the extent of skin lesions. Patients in the most common "mild to moderate" category are usually treated with topical agents which are regarded as first line therapy in this patient group. The two most common groups of prescription drugs are topical steroids and vitamin D analogues. While there are a number of these topical psoriasis treatments on the market today, many have limited efficacy or side-effect profiles, which restrict their usefulness.

ATL1101 is a second-generation antisense drug designed to silence, or suppress, the gene for the insulinlike growth factor-I receptor (IGF-Ir). IGF-Ir's pivotal role in the regulation of cell over-growth in Psoriasis was established by our research partner, the Murdoch Childrens Research Institute. ATL1101 is being developed as a cream treatment for mild-to-moderate cases of Psoriasis.

The Psoriasis project is supported by a Commonwealth Government R&D Start grant of \$1.1 million.

#### **Progress**

In July 2003, Antisense Therapeutics announced its plans to undertake a "proof of concept" study that will accelerate the testing of ATL1101 in humans suffering from Psoriasis. In this "proof of concept" study, also referred to as the Small Plaque Assay (SPA), a relatively small quantity of ATL1101 will be applied to areas of psoriatic skin on a limited number of patients. The SPA is designed to carefully monitor and also restrict the extent of patients' exposure to the test compound.

Typically a drug's activity is not established until completion of Phase II clinical trials. However, a "proof of concept" study of ATL1101 can be undertaken relatively inexpensively for a disease such as Psoriasis (unlike for many other diseases), which will provide early evidence of activity. While the SPA will not replace the requirement to undertake formal (Phase I, II and III) human clinical trials, if early indications of activity are shown, the company will have increased confidence in the prospects for successful commercial development of ATL1101.

The manufacture of the active pharmaceutical ingredient and formulation of the injectable and cream presentations of ATL1101 for use in the "proof-of-concept" study were completed during the period under review. The required precursory toxicology programmes to support this study also commenced on schedule.

As at the end of June 2004 Antisense Therapeutics and MCRI concluded their research agreement, marking the successful completion of pre-clinical research on ATL1101 for psoriasis. Investigation of the application of ATL1101 in other skin disorders will be carried out by Antisense Therapeutics' researchers at its newly established research laboratory. See section headed "Other Research Projects" below.

#### Outlook

Assuming toxicology studies are successfully completed, an application for approval to commence the SPA will be prepared and submitted. Subject to receiving the relevant approvals to conduct the study, the human "proof of concept" study is expected to begin in late 2004.

#### New Development Project - Growth and Sight Disorders (ATL1103)

#### Results of Animal Studies & About The Diseases

In February 2004 the company announced that it is developing a new antisense compound, codenamed ATL1103, designed to block Growth Hormone receptor (GHr) expression. Successful testing undertaken in mice indicates it has potential as a treatment for diseases associated with excessive growth hormone action. These diseases include acromegaly (an abnormal growth disorder of organs, face, hands and feet), diabetic retinopathy and wet age-related macular degeneration (AMD). The latter disorders are common diseases of the eye and major causes of blindness.

#### About Acromegaly

Acromegaly is a serious chronic life shortening disease triggered by excess secretion of growth hormone (GH) by benign pituitary tumours. Oversupply of GH overstimulates liver, fat and kidney cells, through their GH receptors, to produce excess levels of Insulin-Like Growth Factor-I (IGF-I) in the blood manifesting in abnormal growth of the face, hands and feet, and enlargement of body organs including liver, kidney and heart. The primary treatments for acromegaly are to surgically remove the pituitary gland and/or drug therapy to normalize GH and serum IGF-I levels.

#### About Diabetic Retinopathy and Age Related Macular Degeneration (AMD)

Diabetic retinopathy and wet age-related macular degeneration (AMD) are two of the leading causes of vision loss. Over 5 million Americans aged 18 and older are affected by diabetic retinopathy. Around 12,000-24,000 patients with diabetic retinopathy lose their eyesight each year in the US alone. These conditions are caused by new blood vessel formation in the retina or macula (the central part of the retina). In diabetes, high blood glucose can cause oxygen deprivation, which can stimulate factors that induce additional blood vessels in the retina. In AMD similar factors are thought to stimulate blood vessel production in the macula. These new blood vessels may break and bleed into the eye leading to scarring within the eye. Whilst there are drugs to control diabetes, patients with Type I diabetes who have had their disease for more than 10 years have a 90% chance of developing retinopathy, and about 20% of patients with Type II diabetes will get the disease. Surgical ablative treatments such as photocoagulation (laser therapy) are available but are not completely effective, may cause partial vision loss, and can only be used a limited number of times.

The targeting of GHr with Antisense Therapeutics' proprietary antisense compound (ATL1103) inhibits growth hormone activity, thereby reducing levels of the hormone insulin-like growth factor-I (IGF-I) in the blood. Acromegalic patients are known to have significantly higher blood IGF-I levels than healthy individuals. Reduction of these levels to normal is accepted by clinical authorities as the primary marker of an effective drug treatment for the disease. In the case of diabetic retinopathy, published clinical studies have shown that treatments producing a reduction in IGF-I levels retarded the progression of the disease in patients.

Antisense Therapeutics' animal studies for the GHr antisense compound were conducted at the University of Queensland by Professor Michael Waters, internationally recognised for his research on GHr and disorders related thereto. These studies demonstrated that the compound significantly reduces blood levels of IGF-I in mice, an effect which, if reproduced in humans, should provide therapeutic benefit to acromegaly patients and potentially to diabetic retinopathy sufferers.

The animal study results for ATL1103 were presented by Antisense Therapeutics to an International GH-IGF Symposium in Cairns in April 2004.

Growth and Sight Disorders - Markets, Current Treatments

The most widely used pharmaceutical treatment for acromegaly is the drug octreotide (Sandostatin<sup>TM</sup>), however a significant percentage of patients do not respond to this therapy while other patients experience adverse reactions with this therapy. The latest drug to be approved in Europe and the US for the treatment of acromegaly is pegvisomant (Trovert<sup>TM</sup>, Somavert<sup>TM</sup>). Pegvisomant is effective in a larger percentage of patients than octreotide although it requires more frequent (daily) dosing by injection than the long acting form of octreotide which is surgically implanted (intragluteal).

In North America, Europe and Japan there are approximately 40,000 diagnosed acromegaly patients with about half requiring drug therapy. Drug treatment costs vary depending on dosage and frequency of administration ranging from A\$14,000-\$33,000 per patient per year

The study results for ATL1103 are comparable to those achieved by pegvisomant in an equivalent animal model. ATL1103 may have important clinical advantages over pegvisomant and octreotide, including more convenient route of administration and less frequent dosing.

There are presently no pharmaceutical therapeutics approved for the treatment of diabetic retinopathy. There are also no standard and effective therapies for most AMD patients. Given the high unmet medical need for such diseases the market potential for effective medicines is estimated to be several billion dollars.

Patent applications have been lodged covering all disease indications for GHr antisense.

#### Outlook

Orders for bulk quantities of the active pharmaceutical ingredient, to be formulated into injectable product for use in the preclinical safety studies, are expected to be placed with our collaboration partner Isis Pharmaceuticals Inc within the second half of 2004.

#### Other Research Projects

#### Background

Antisense Therapeutics is focusing on projects that target growth and vision disorders and major inflammatory diseases.

The company has agreed a list of key research targets with Isis, and can during the research and development phase, select a certain number of those with the most potential to exclusively commercialise.

As stated earlier, the company has acquired from Isis an exclusive right to research these targets using the Isis technology, and in accordance with the Antisense Therapeutics/Isis agreements, antisense compounds to these targets are being created by Isis for Antisense Therapeutics. Antisense Therapeutics is contracting with local and international groups who are experts at testing drugs in their validated animal models to assess the efficacy of these antisense compounds.

# Progress

Moving the ATL1103 project into development from the company's drug research pipeline during the year has demonstrated Antisense Therapeutics' ability to use the most advanced second-generation antisense technology to quickly and inexpensively generate and test new antisense compounds for clinically validated targets in important human diseases.

In July 2004 the company announced the establishment of a new laboratory to support its research effort. The laboratory is located in new research & development facilities at the Murdoch Childrens Research Institute (MCRI). The laboratory will support the company's antisense drug research pipeline, by conducting the antisense-specific aspects of each of the company's animal research projects.

#### Outlook

Following completion of the efficacy studies currently in progress and of those to commence during the 2004/2005 financial year, Antisense Therapeutics will critically assess their results and determine on a

case by case basis whether further development work will be undertaken by the company or alternatively out-license to other pharmaceutical companies in return for licensing income.

# **Partnering Opportunities**

As stated earlier, the company's strategy is to commercialise its drug pipeline products through collaborations with major pharmaceutical companies. The company expects there to be interest from potential partners in both ATL1101 and ATL1102 given the quality of the targets and the known commercial appeal of antisense, and on the assumption that the compounds will continue to progress successfully through development. Presently our plans are to partner ATL1101 and ATL1102, assuming successful results, after the completion of the "proof of concept' study in psoriasis patients and the Phase IIa trial in MS patients respectively.

The company continues to communicate directly, and on a regular basis, with selected interested companies in order to update them on the development status of Antisense Therapeutics' lead compounds and to broaden the awareness of the company's activities in preparation for potential future licensing or other partnership discussions.

#### Financial Position

As stated in the Director's Report the company's current cash reserves are expected to be sufficient to fund activities for at least the next twelve months. In order for the company to accelerate certain existing development programs and/or progress potential new project opportunities, the company will be required to raise further capital.

In relation to the proposed use of funds described above, it should be recognised that there will typically be differences between the forecast and actual results, because events and circumstances frequently do not occur as expected, and those differences may be material.

# Biotechnology Companies - Inherent Risks

Some of the risks inherent in the development of a product to a marketable stage include the uncertainty of patent protection and proprietary rights, whether patent applications and issued patents will offer adequate protection to enable product development, the obtaining of the necessary drug regulatory authority approvals and difficulties caused by the rapid advancements in technology. Also a particular compound may fail the clinical development process through lack of efficacy or safety. Companies such as Antisense Therapeutics Limited are dependent on the success of their research projects and on the ability to attract funding to support these activities. Investment in research and development projects cannot be assessed on the same fundamentals as trading and manufacturing enterprises. Thus investment in these areas must be regarded as speculative taking into account these considerations.

This annual report may contain forward-looking statements regarding the potential of the company's projects and interests and the development and therapeutic potential of the company's research and development. Any statement describing a goal, expectation, intention or belief of the company is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercialising drugs that are safe and effective for use as human therapeutics and the financing of such activities. There is no guarantee that the company's research and development projects will be successful or receive regulatory approvals or prove to be commercially successful in the future. Actual results of further research could differ from those projected or detailed in this report. As a result, you are cautioned not to rely on forward-looking statements. Consideration should be given to these and other risks concerning the company's research and development program referred to in this Operations Report and in the company's Directors' Report as contained in this annual report for the year ended 30 June 2004.

# Antisense Therapeutics Limited ABN 41 095 060 745

Annual Financial Report for the year ended 30 June 2004



■ 120 Collins Street Melbourne VIC 3000 Australia

GPO Box 67 Melbaume VIC 3001 Fax 61 3 9288 8000 Fax 61 3 9654 6166 DX 293 Melbourne

# Independent audit report to members of Antisense Therapeutics Limited

# Scope

The financial report and directors' responsibility

The financial report comprises the statement of financial position, statement of financial performance, statement of cash flows, accompanying notes to the financial statements, and the directors' declaration for Antisense Therapeutics Limited (the company), for the year ended 30 June 2004.

The directors of the company are responsible for preparing a financial report that gives a true and fair view of the financial position and performance of the company, and that complies with Accounting Standards in Australia, in accordance with the *Corporations Act 2001*. This includes responsibility for the maintenance of adequate accounting records and internal controls that are designed to prevent and detect fraud and error, and for the accounting policies and accounting estimates inherent in the financial report.

# Audit approach

We conducted an independent audit of the financial report in order to express an opinion on it to the members of the company. Our audit was conducted in accordance with Australian Auditing Standards in order to provide reasonable assurance as to whether the financial report is free of material misstatement. The nature of an audit is influenced by factors such as the use of professional judgement, selective testing, the inherent limitations of internal control, and the availability of persuasive rather than conclusive evidence. Therefore, an audit cannot guarantee that all material misstatements have been detected.

We performed procedures to assess whether in all material respects the financial report presents fairly, in accordance with the *Corporations Act 2001*, including compliance with Accounting Standards in Australia, and other mandatory financial reporting requirements in Australia, a view which is consistent with our understanding of the company's financial position, and of its performance as represented by the results of its operations and cash flows.

We formed our audit opinion on the basis of these procedures, which included:

- examining, on a test basis, information to provide evidence supporting the amounts and disclosures in the financial report, and
- assessing the appropriateness of the accounting policies and disclosures used and the reasonableness of significant accounting estimates made by the directors.

While we considered the effectiveness of management's internal controls over financial reporting when determining the nature and extent of our procedures, our audit was not designed to provide assurance on internal controls.

We performed procedures to assess whether the substance of business transactions was accurately reflected in the financial report. These and our other procedures did not include consideration or judgement of the appropriateness or reasonableness of the business plans or strategies adopted by the directors and management of the company.

# Independence

We are independent of the company, and have met the independence requirements of Australian professional ethical pronouncements and the *Corporations Act 2001*. In addition to our audit of the financial report, we were engaged to undertake the services disclosed in the notes to the financial statements. The provision of these services has not impaired our independence.

# Audit opinion

In our opinion, the financial report of Antisense Therapeutics Limited is in accordance with:

- (a) the Corporations Act 2001, including:
  - (i) giving a true and fair view of the financial position of Antisense Therapeutics Limited at 30 June 2004 and of its performance for the year ended on that date; and
  - (ii) complying with Accounting Standards in Australia and the Corporations Regulations 2001; and
- (b) other mandatory financial reporting requirements in Australia.

Ernst & Young

Emsto To

Denis Thorn

Partner

Melbourne

26 August 2004

# **Contents**

Statement of Financial Position	2
Statement of Financial Performance	3
Statement of Cash Flows	4
Notes to the Financial Statements	5
Directors' Declaration	23

i

# **Statement of Financial Position**

AT 30 JUNE 2004	Note	2004 \$	2003 \$
CURRENT ASSETS			
Cash assets	15(a)	14,421,232	6,545,567
Receivables	3	222,129	68,730
Other	4	299,920	878,941
Total Current Assets		14,943,281	7,493,238
NON-CURRENT ASSETS			
Plant & equipment	5	47,350	50,911
Intangible assets	6	3,160,500	4,438,000
Total Non-Current Assets		3,207,850	4,488,911
Total Assets		18,151,131	11,982,149
CURRENT LIABILITIES			
Payables	7	879,636	326,302
Provisions	8	138,512	38,101
Total Current Liabilities		1,018,148	364,403
Total Liabilities		1,018,148	364,403
Net Assets		17,132,983	11,617,746
EQUITY			
Contributed equity	9	33,839,365	23,714,504
Reserves	10	725,885	725,885
Accumulated losses	11	(17,432,267)	(12,822,643)
Total Equity		17,132,983	11,617,746

# **Statement of Financial Performance**

FOR THE YEAR ENDED 30 JUNE 2004	Note	2004 \$	2003 \$
Revenue from ordinary activities	2	1,341,377	448,066
Administrative expenses		(1,107,037)	(1,028,248)
Occupancy expenses		(75,258)	(46,829)
Patent expenses		(39,673)	(25,295)
Research and development expenses		(3,823,353)	(4,172,812)
Amortisation expense	2	(1,277,500)	(1,277,500)
Other expenses from ordinary activities	2	•	(5,280)
Loss from ordinary activities before income tax benefit	,	(4,981,444)	(6,107,898)
Income tax benefit relating to ordinary activities	12	371,820	-
Loss from ordinary activities after related income tax benefit		(4,609,624)	(6,107,898)
Net loss	11	(4,609,624)	(6,107,898)
Share issue costs	9	(271,899)	(277,359)
Total revenues, expenses and valuation adjustments attributable to members of Antisense Therapeutics Limited and			
recognised directly in equity		(271,899)	(277,359)
Total changes in equity other than those resulting from transactions with owners as owners		(4,881,523)	(6,385,257)
Basic earnings (loss) per share (cents per share)	14	(1.37)	(2.46)
Diluted earnings (loss) per share (cents per share)	14	(1.37)	(2.46)

# **Statement of Cash Flows**

FOR THE YEAR ENDED 30 JUNE 2004	Note 2004 \$		2003 \$
CASH FLOWS FROM OPERATING ACTIVITIES:			
Payments to suppliers, employees and for research and			
development		(4,082,154)	(7,351,299)
Interest received		667,498	352,771
Bank finance charges		(3,572)	(1,488)
Grant income received		836,800	-
Income tax refund	_	371,820	
Net cash flows used in operating activities	15(b)	(2,209,608)	(7,000,016)
CASH FLOWS FROM INVESTING ACTIVITIES:			
Purchase of property, plant and equipment		(17,661)	(23,332)
Proceeds from sale of plant and equipment		-	1,680
Net cash flows used in investing activities	-	(17,661)	(21,652)
CASH FLOWS FROM FINANCING ACTIVITIES:			
Proceeds from issue of shares and options		10,396,760	4,521,291
Payment of share and option issue costs		(293,826)	(327,106)
Net cash flows from financing activities	-	10,102,934	4,194,185
Net increase/(decrease) in cash held		7,875,665	(2,827,483)
Cash at the beginning of the financial year		6,545,567	9,373,050
Cash at the end of the financial year	15(a)	14,421,232	6,545,567

# **Notes to the Financial Statements**

#### FOR THE YEAR ENDED 30 JUNE 2004

#### NOTE 1 STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES

#### (i) Basis of Accounting

The financial report is a general-purpose financial report, which has been prepared in accordance with the requirements of the Corporations Act 2001 including applicable accounting standards. Other mandatory professional reporting requirements (Urgent Issues Group Consensus Views) have also been complied with.

The financial report has also been prepared in accordance with the historical cost convention.

#### (ii) Changes in accounting policies

The accounting policies adopted are consistent with those of the previous year.

#### (iii) Income Tax

The financial statements apply the principles of tax-effect accounting. The income tax benefit in the Statement of Financial Performance represents the tax on pre-tax accounting loss adjusted for income and expenses never to be assessed or allowed for taxation purposes. The provision for deferred income tax liability and future income tax benefit (as disclosed, but not recognised in the Statement of Financial Position) include the tax effect of differences between income and expenses recognised in different accounting periods for book and tax purposes, calculated at the tax rates expected to apply when the differences reverse.

The future income tax benefits relating to tax losses and timing differences have not been recognised as an asset as there is no virtual certainty of realisation, except for tax rebates received under the Research & Development Tax Concession of the Income Tax Assessment Act 1936.

#### (iv) Goods and Services Tax

Revenues, expenses and assets are recognised net of the amount of GST except:

- where the GST incurred on a purchase of goods and services is not recoverable from the taxation authority, in
  which case the GST is recognised as part of the cost of acquisition of the asset or as part of the expense item as
  applicable; and
- receivables and payables are stated with the amount of GST included.

Cash flows arising from operating activities are included in the Statement of Cash Flows on a gross basis (i.e. including GST) and the GST component of cash flows arising from investing and financing activities, which is recoverable from, or payable to, the taxation authority are classified as operating cash flows. Commitments and contingencies are disclosed net of the amount of GST recoverable from, or payable to, the taxation authority.

#### (v) Plant and Equipment

Plant and equipment are measured at cost and are depreciated over their useful economic lives as follows:

	Life	Method
Equipment and furniture	3-5 years	Straight line

#### NOTE 1 STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

#### (vi) Recoverable amounts of non-current assets

Non-current assets measured using the cost basis are not carried at an amount above their recoverable amount, and where a carrying value exceeds this recoverable amount, the asset is written down. In determining the recoverable amount, the expected cash flows have not been discounted.

#### (vii) Research and Development

Research and development costs and patent costs are expensed as incurred, except where future benefits are expected, beyond any reasonable doubt. Where research and development costs are deferred such costs are amortised over future periods on a basis related to expected future benefits. Unamortised costs are reviewed at each balance date to determine the amount (if any) that is no longer recoverable and any amount identified is written off.

#### (viii) Employee Benefits

Provision is made for employee benefits accumulated as a result of employees rendering services up to the reporting date. These benefits include wages and salaries, annual leave and long service leave.

Liabilities arising in respect of wages and salaries, annual leave, sick leave and any other employee benefits expected to be settled within twelve months of the reporting date are measured at their nominal amounts based on remuneration rates which are expected to be paid when the liability is settled. All other employee benefit liabilities are measured at the present value of the estimated future cash outflow to be made in respect of services provided by employees up to the reporting date. In determining the present value of future cash outflows, the market yield as at the reporting date on national government bonds, which have terms to maturity approximating the terms of the related liability, are used.

Employee benefit expenses and revenues arising in respect of the following categories:

- wages and salaries, non-monetary benefits, annual leave, long service leave, sick leave and other leave benefits; and
- · other types of employee benefits

are recognised against profits/losses on a net basis in their respective categories.

The value of the equity-based compensation scheme described in note 19 is not being recognised as an employee benefits expense.

#### (ix) Employee Option Ownership Schemes

Certain employees are entitled to participate in option ownership schemes. The details of the schemes are described in Note 19. No remuneration expense is recognised in respect of employee options issued.

#### (x) Financial Instruments Included in Equity

Ordinary share capital is recorded at the amount received on issue, less any share issue costs. Ordinary share capital bears no special terms or conditions affecting income or capital entitlements of the shareholders.

#### (xi) Financial Instruments Included in Assets

Cash in bank and short-term deposits are stated at nominal value. Interest revenue is recognised on an effective yield basis.

#### NOTE 1 STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

#### (xii) Foreign Currencies

Transactions in foreign currencies are converted to local currency at the rate of exchange ruling at the date of the transaction

Amounts payable to and by the company outstanding at reporting date and denominated in foreign currencies have been converted to local currency using rates prevailing at the end of the financial year.

#### (xiii) Earnings per share

Basic EPS is calculated as net loss attributable to members, adjusted to exclude costs of servicing equity (other than dividends), divided by the weighted average number of ordinary shares, adjusted for any bonus element.

Diluted EPS is calculated as net loss attributable to members, adjusted for:

- costs of servicing equity (other than dividends);
- the after tax effect of dividends and interest associated with dilutive potential ordinary shares that have been recognised as expenses; and
- other non-discretionary changes in revenues or expenses during the period that would result from the dilution of potential ordinary shares;

divided by the weighted average number of ordinary shares and dilutive potential ordinary shares, adjusted for any bonus element.

#### (xiv) Operating Leases

The minimum lease payments of operating leases, where the lessor effectively retains substantially all of the risks and benefits of ownership of the leased item, are recognised as an expense on a straight-line basis.

#### (xv) Intangible assets

Intangible assets are amortised on a straight line basis over the term of the rights granted, which is currently expected to be five years. The unamortised balance of intangible assets is reviewed at each balance date and charged to the Statement of Financial Performance to the extent that applicable future benefits are no longer probable.

#### (xvi) Payables

Liabilities for trade creditors and other amounts are carried at cost, which is the fair value of the consideration to be paid in the future for goods and services received, whether or not billed to the company.

#### (xvii) Borrowing costs

Borrowing costs are expensed as incurred.

#### (xviii) Contributed Equity

Issued and paid up capital is recognised at the fair value of the consideration received by the company. Any transaction costs arising on the issue of ordinary shares are recognised directly in equity as a reduction of the share proceeds received.

# NOTE 1 STATEMENT OF SIGNIFICANT ACCOUNTING POLICIES (CONTINUED)

#### (xix) Revenue Recognition

Revenue is recognised to the extent that it is probable that the economic benefits will flow to the entity and the revenue can be reliably measured. The following specific recognition criteria must also be met before revenue is recognised:

Interest

Control of the right to receive the interest payment.

Government Grants

Control of the right to receive the grant from the government.

# (xx) Cash and Cash Equivalents

Cash on hand and in banks and short-term deposits are stated at nominal value.

NOTE 2.	REVENUE AND EXPENSES	2004 \$	2003 \$
Revenues	from ordinary activities:	<b>y</b>	<b></b>
	m external parties	673,795	355,029
Start grant	<u>-</u>	692,375	-
Foreign exc	change gains / (losses)	•	
- Unreali		(24,630)	16,832
- Realise	d	(163)	74,525
Proceeds fr	om the disposal of plant and equipment (a)	•	1,680
Total reve	nues from ordinary activities	1,341,377	448,066
Expenses a	and Losses:		
Depreciation	on of:		
- Equipm	ent and furniture	21,222	18,854
Operating 1	lease rentals:		
- Minimu	ım lease payments	61,240	39,475
Amortisation	on of intangibles	1,277,500	1,277,500
Other expe	nses comprising of:		
	down value of plant and equipment (a)	-	5,280
(a) Nas	less on disposal of alast and assistant		2.600
(a) Net	loss on disposal of plant and equipment	•	3,600

	2004 \$	2003 \$	
NOTE 3. RECEIVABLES (CURRENT)			
Interest receivable - bank	49,522	43,225	
Input tax credits	39,360	25,351	
TFN withholding tax	•	154	
Other receivables	133,247	•	
Total receivables	222,129	68,730	
NOTE 4. OTHER ASSETS (CURRENT)			
Prepayments	291,577	873,294	
Other	8,343	5,647	
Total other assets	299,920	878,941	
NOTE 5. PLANT AND EQUIPMENT			
Equipment and furniture at cost			
Opening balance	78,549	63,645	
Additions	17,661	22,605	
Disposals		(7,701)	
Closing balance	96,210	78,549	
Accumulated Depreciation			
Opening balance	(27,638)	(11,205)	
Depreciation for the period	(21,222)	(18,854)	
Disposals	<u>-</u>	2,421	
Closing balance	(48,860)	(27,638)	
Net book value	47,350	50,911	

NOTE 6. INTANGIBLE ASSETS	2004 \$	2003
Intellectual property (a)	6,387,500	6,387,500
Accumulated amortisation	(3,227,000)	(1,949,500)
Closing balance	3,160,500	4,438,000

- (a) The intangible assets relate to certain rights granted to Antisense Therapeutics Limited by Isis Pharmaceuticals Inc. and The Murdoch Childrens Research Institute upon listing of the company. The main features of the agreements with the aforementioned entities, respectively, are as follows:
  - Isis Pharmaceuticals Inc. ("Isis") has granted Antisense Therapeutics Limited rights to use Isis technology (i.e. Isis' patented technology) to commercialise antisense drugs to a number of protein targets (i.e. a research licence for each protein target). A certain number of these research licences to protein targets are also extendible to commercialisation licences.

The agreements with Isis provide access to and assistance in expanding Antisense Therapeutics Limited's drug pipeline and also provide access to and assistance in the company's development projects including an exclusive license to a multiple sclerosis drug in Isis' preclinical pipeline; access to Isis manufacturing for provision of bulk quantities of antisense compounds for clinical trials; and access to Isis' preclinical development services for a sufficient period to allow smooth technology transfer.

Antisense Therapeutics Limited's agreement with the Murdoch Childrens Research Institute provides the
company with worldwide exclusive licences to patents covering antisense directed at a certain target for
dermatological applications including psoriasis.

#### NOTE 7. PAYABLES (CURRENT)

Accounts payable	94,564	69,758
Accrued expenses (unsecured) (a)	783,898	256,544
Other payables	1,174	· -
Total current payables	879,636	326,302
(a) Accrued expenses are non-interest bearing and are normally NOTE 8. PROVISIONS (CURRENT)	settled on 30 day terms.	
Employee benefits	138,512	38,101

NOTE 9. CONTRIBUTED EQUITY		2004 \$		2003
Ordinary Shares Fully Paid		33,839,	365 23	3,714,504
(a) Movement in Issued Shares				
	200	4	200	3
	No of Shares	\$	No of Shares	\$
Balance at beginning of year	275,281,608	23,714,504	215,003,110	19,470,572
Issued during the year (i)	79,969,842	10,396,000	60,275,268	4,520,645
Transaction costs arising on share issues	-	(271,899)	-	(277,359)
Exercise of options	3,800	760	3,230	646
Balance at year end	355,255,250	33,839,365	275,281,608	23,714,504

- (i) The following shares were issued during the period:
  - 30,771,540 fully paid ordinary shares at 13 cents per share in a placement of shares to Australian institutions and professional investors;
  - 41,508,302 fully paid ordinary shares at 13 cents per share to eligible shareholders pursuant to the company's share purchase plan; and
  - 7,690,000 fully paid ordinary shares at 13 cents per share to Polychip Pharmaceuticals Pty Ltd.

	2004 \$	2003 \$
NOTE 10. RESERVES	•	•
Option Reserve	725,885	725,885
(a) Movement in Option Reserve		

#### 2004 2003 No of No of Options **Options** Balance at beginning of period 125,419,665 725,885 125,422,895 725,885 Issued during the period Less costs Exercise of options (3,800)(3,230)(250,000)Options expired Balance at period end 725,885 125,419,665 125,165,865

# NOTE 10. RESERVES (CONTINUED)

# (b) Options over Ordinary Shares

2004

	No of Options				
Date of Issue	26/02/02	19/12/01	3/12/01	15/11/01	15/11/01
On issue at beginning of year ('000)	58,969	32,500	11,950	2,000	20,000
Issued during the year ('000)	- (4)	•	-	-	-
Exercised during the year ('000) Expired during the year ('000)	(4)	-	250	•	
Outstanding at balance date ('000)	58,965	32,500	11,700	2,000	20,000
Exercised subsequent to balance date ('000)	-	-	-	-	-
Outstanding at date of Directors' report ('000)	58,965	32,500	11,700	2,000	20,000
Number of recipients	5,076	1,240	9	1	1
Exercise price	\$0.20	\$0.20	\$0.20	\$0.20	\$0.20
Exercise period from To (expiration day)	26 Feb 2002 1 Feb 2007	19 Dec 2001 1 Feb 2007	3 Dec 2001 31 Jul 2005	15 Nov 2001 31 Jul 2005	15 Nov 2001 30 Nov 2006
The following proportion of options vest from the dates shown:					
100%	26 Feb 2002	19 Dec 2001			15 Nov 2001
20%			1 Aug 2002	1 Aug 2002	
40%			1 Aug 2003	1 Aug 2003	
40%			1 Aug 2004	1 Aug 2004	
			200 \$	4	2003 \$
NOTE 11. ACCUMULATED LOSSES					
Accumulated losses at the beginning of the fine Net loss				9,624)	(6,714,745) (6,107,898)
Accumulated losses at the end of the financial	year		(17,43	2,267)	(12,822,643)

	2004	2003
NOTE 12. INCOME TAX	\$	\$
The prima facie tax, using the tax rate applicable in the country of operation, on loss differs from the income tax provided in the financial statements as follows:		
Loss from ordinary activities	(4,609,624)	(6,107,898)
Prima facie income tax benefit calculated at 30%	(1,382,887)	(1,832,369)
Tax effect of permanent and other differences:		
Research and development R&D start grant clawback Amortisation of intellectual property Amortisation of equity raising costs Amount (over)/under provided in prior years Other	(80,814) 84,039 383,250 (79,769) (5,570) 487	(77,569) 383,250 (67,360) 316,519 312
Income tax benefit adjusted for permanent and other differences	(1,081,264)	(1,277,217)
Benefit of tax losses not brought to account  Total income tax benefit attributable to operating loss (a)	709,444 (371,820)	1,277,217
The estimated potential future income tax benefit at period end calculated at 30% in respect of tax losses not brought to account is:	4,242,398	3,151,839

(a) The income tax benefit comprises cash rebates received/receivable which are available under the Research and Development Tax Concession of the Income Tax Assessment Act 1936.

The estimated potential future income tax benefit not recognised at period end in respect of timing differences for the company amounted to \$6,057 (2003: (\$4,082)).

The benefits of the tax losses and timing differences will only be realised if:

- (i) the company derives future assessable income of a nature and amount sufficient to enable the benefit of the taxation deductions to be realised;
- (ii) the company continues to comply with the conditions for deductibility imposed by law; and
- (iii) there are no changes in taxation legislation adversely affecting the company in realising the benefit from the deductions for the losses.

	2004 \$	2003 \$
NOTE 13. FOREIGN CURRENCIES	3	<b>.</b>
Amounts payable/receivable in foreign currencies The Australian dollar equivalents of unhedged amounts payable or receivable in foreign currencies, calculated at year end exchange rates as follows:		
US Dollars Amounts payable: Euro	574,954	176,140
Amounts payable:	10,548	51,575
NOTE 14. EARNINGS PER SHARE		
Basic Earnings Per Share (cents per share) Diluted Earnings Per Share (cents per share)	(1.37) (1.37)	(2.46) (2.46)
The following reflects the income and share data used in the calculations of basic and diluted earnings per share:		
(a) Loss used in calculating basic and diluted earnings per share (numerator)	(4,609,624)	(6,107,897)
(b) Number of Ordinary Shares Weighted average number of ordinary shares on issue used in the calculation of basic earnings per share (denominator)	336,724,809	248,258,386
(c) Potential Ordinary Shares Not Considered Dilutive All potential ordinary shares, being options to acquire ordinary shares ended 30 June 2004.	, are not considered	d dilutive for the year

#### NOTE 15. NOTES TO THE STATEMENT OF CASH FLOWS

#### (a) Reconciliation of Cash

For the purpose of the Statement of Cash Flows, cash includes cash at bank and deposits at call. Cash at the end of the period as shown in the Statement of Cash Flows is reconciled to the related items in the Statement of Financial Position as follows:

Cash at bank	3,921,232	1,545,567
Term deposits (i)	10,500,000	5,000,000
	14,421,232	6,545,567

There have been no other conversions to, calls of, or subscription for ordinary shares or issues of potential

ordinary shares since the reporting date and before the completion of this financial report.

(i) Term deposits are with a major bank and are short term. The bank pays interest at current bank deposit rates. At year end the average rate was 5.3%.

(d)

	2004 \$	2003 \$
NOTE 15. NOTES TO THE STATEMENT OF CASH FLO	OWS (CONTINUED)	
(b) Reconciliation of the net loss after tax to the net cash f	lows from operations	
Net loss	(4,609,624)	(6,107,898)
Non-cash items		
Unrealised foreign exchange (gain) / loss	24,630	(16,832)
Amortisation of intangibles	1,277,500	1,277,500
Depreciation expense	21,222	18,854
Loss on disposal of asset	-	3,600
Changes in assets and liabilities		
(Increase) decrease in current receivables	(153,399)	(15,534)
(Increase) decrease in other current assets	579,020	(738,911)
Increase (decrease) in payables	550,632	(1,443,480)
Increase (decrease) in employee provisions	100,411	22,686
Net operating cash flows	(2,209,608)	(7,000,016)

#### NOTE 16. DIRECTOR AND EXECUTIVE DISCLOSURES

#### (a) Details of Specified Directors and Specified Executives

# (i) Specified Directors

R W Moses	Chairman (non-executive)
M Diamond	Managing Director
C Belyea	Director (non-executive)
S Crooke	Director (non-executive)
G Mitchell	Director (non-executive)
G Werther	Director (non-executive)

#### (ii) Specified Executives

J Iswaran	Development Director
C Wraight	Research Director
G Tachas	Director, Drug Discovery & Patents
K Andrews	Chief Financial Officer
N Korchev	Company Secretary

#### (b) Remuneration of Specified Directors and Specified Executives

#### (i) Remuneration Policy

The Remuneration Committee of the Board of Directors of Antisense Therapeutics Limited is responsible for overseeing the remuneration policy of the Company and for recommending or making such changes to the policy as it deems appropriate. The Committee's objective in overseeing the remuneration policy is to enable the Company to attract, motivate and retain suitably experienced directors and senior management who will create value for shareholders.

The remuneration policy ensures that directors and senior management are appropriately remunerated having regard to their relevant experience, performance, the performance of the Company, industry norms/standards and the general pay environment as appropriate.

To assist in achieving these objectives, the remuneration policy links certain conditions of executive directors' and officers remuneration to the Company's financial and operational performance. For executive directors and officers, remuneration packages comprise salary and superannuation and all executives are entitled to participate in the Employee Short Term Incentive Scheme which provides for annual cash bonuses for excellent performance in the achievement of key corporate and individual objectives. Executives may also be provided with longer-term incentives through the Company's Employee Option Plan, to allow the executives to participate in the growth of the Company as a result of their efforts and to assist in the retention of these key employees.

Specified Directors	Primai	гу	Post Employment	Equity	Total
	Salary & Fe	es Cash Bonus	Superannuation	Options	
R Moses					
2004	35,000		3,150	46	38,196
2003	35,000		3,150	45	38,195
M Diamond					
2004	212,502	15,000	19,125	549	247,177
2003	200,004		18,000	544	218,548
C Belyea					
2004	25,000		2,250	366	27,616
2003	25,000		2,250	362	27,612
S Crooke					
2004	25,000			366	25,366
2003	25,000			362	25,362
G Mitchell					
2004	25,000		2,250	46	27,296
2003	25,000		2,250	45	27,295
G Werther					
2004	25,000		2,250	366	27,616
2003	25,000		2,250	362	27,612
Total Remuneration: Spec	ified Directors				
2004	347,502	15,000	29,025	1,739	393,267
2003	335,004	•	27,900	1,720	364,624

Specified Executives		Primary	P	ost Employment	Equity	Total
		Salary & Fees	Cash	Superannuation	Options	
			Bonus			
J Iswaran						
	2004	171,667		15,450	92	187,209
	2003	150,000		13,500	91	163,591
C Wraight						
	2004	170,000		15,300		185,300
	2003	85,000		7,650		92,650
G Tachas						
	2004	154,500		13,905	275	168,680
	2003	151,125		13,601	272	164,998
K Andrews						
	2004	69,129		6,211		75,340
	2003	55,205		4,968		60,173
N Korchev						
	2004	25,000		2,250	37	27,287
	2003	25,000		2,250	36	27,286
Total Remuner	ation: Specifi	ed Executives				
	2004	590,296		53,116	404	643,816
	2003	466,330		41,969	399	508,698
	2003	400,550		41,505	377	500,07

- (c) Options granted and vested during the year
- (i) Options granted during the year

No options were granted to directors and officers during the year ended 30 June 2004.

(ii) Options vested during the year

Options issued by Antisense Therapeutics Limited in 2002 have 3 vesting dates, for various proportions of the total issued options, during the life of the options as detailed below. Accordingly, although no options were issued during the year ended 30 June 2004, the options issued to directors and specified executives in previous years, which had not vested at 1 July 2003, have been allocated a total value of \$2,143 for the current financial year and are included in the remuneration of directors and specified executives above. This amount has been determined by allocating the fair value of options issued equally over the vesting periods. Currently, the amortised fair value is not recognised as an expense in the financial statements and no adjustments have been made to reflect estimated or actual forfeitures (ie. options that do not vest or are not exercised).

Details relating to options issued and the valuation basis adopted are as follows:

As stated in the company's 2002 annual report:

9,500,000 options were granted to directors during the 2002 financial year. "Each option entitles the holder to purchase 1 ordinary share in Antisense Therapeutics Limited at an exercise price of 20 cents". There were 2,000,000 options granted on 15 November 2001 and 7,500,000 options granted on 3 December 2001. These options granted to directors are restricted securities and are escrowed for a period of 2 years from the date of official quotation of shares offered under the first prospectus issued by the company or such other period as the Australian Stock Exchange may require. Subject to the escrow arrangements, the option holder may not exercise more than the following proportions of options on the following dates:

<ul> <li>Prior to 31 July 2002</li> </ul>	0%
<ul> <li>Between 1 August 2002 and 31 July 2003</li> </ul>	20%
Between 1 August 2003 and 31 July 2004	60%
<ul> <li>Retween 1 August 2004 and 31 July 2005</li> </ul>	100%

These options had no market value at date of grant and are "out of the money" as at the year end (market price per share \$0.12), whereas as stated above, the options have an exercise price of 20 cents. The directors have endeavoured to estimate the fair values of the options by using the Black-Scholes options pricing formula which values each option based on the expiration date and exercise price. Based on this accepted formula each option has a negligible value of 0.00459 of a cent. The directors have adopted this valuation for the purpose of these accounts. "

All options issued to directors were released from escrow restrictions in December 2003.

2,200,000 options were granted to officers of the company during the 2002 financial year. Each option entitles the holder to purchase 1 ordinary share in Antisense Therapeutics Limited at an exercise price of 20 cents. These options were granted on 3 December 2001 on the same terms as those described above, except that these options are not subject to any escrow arrangements.

These options continue to be "well out of the money" as at the 2004 year-end (market share price \$0.145).

# Values of Options Issued to Directors and Specified Executives - Assumptions

The following assumptions were used to derive a value for the options issued using the Black-Scholes options pricing formula at the 2002 financial year-end date.

#### Options Granted

	15 November 2001	3 December 2001	
Dividend yield	•	-	
Expected volatility	12.34%	12.34%	
Historical volatility	12.34%	12.34%	
Risk-free interest rate	5.622%	5.622%	
Expected life of option	•		

<sup>\*</sup> Assumed to be total years from grant date to expiration date.

# (d) Option holdings of Directors and Specified Executives

	Balance at 1 July 2003	Granted as remuneration	Options Exercised	Net Change Other	Balance at 30 June 2004	Total Exercisable (Vested at 30 June 2004)
Directors			_			
R Moses	375,000	-	-		- 375,000	275,000
M Diamond	3,075,000	-	-		3,075,000	1,875,000
C Belyea (a)	2,337,000	-	-		- 2,337,000	1,537,000
S Crooke (b)	22,000,000	-	-		- 22,000,000	13,200,000
G Mitchell	250,000	-	-		- 250,000	150,000
G Werther	2,012,500	-	-		- 2,012,500	1,212,500
Specified						
Executives						
J Iswaran	625,000	•	-		- 625,000	425,000
C Wraight	2,000,000	-	-		- 2,000,000	1,200,000
G Tachas (c)	1,625,000	-	-		- 1,625,000	1,025,000
K Andrews	-	-	-			-
N Korchev	200,000				- 200,000	120,000
Total	34,499,500	-	-		- 34,499,500	21,019,500

<sup>(</sup>a) 277,000 options held by an entity in which director has a beneficial interest

<sup>(</sup>b) 20,000,000 options held by entity in which director has a beneficial interest

<sup>(</sup>c) 62,500 options held by an entity in which specified executive has a beneficial interest

#### (e) Shareholdings of Directors and Specified Executives

	Balance at 1 July 2003	Granted as Remuneration	Ne	t Change Other	On Exercise of Options	Balance at 30 June 2004
Directors						_
R Moses	250,000		-	38,462		- 288,462
M Diamond	176,666		-	23,077		- 199,743
C Belyea (a)	500,000		-	-		- 500,000
S Crooke (b)	40,333,333		-	-		- 40,333,333
G Mitchell	•		-	-		-
G Werther	25,000		•	1,687,500 (d)		- 1,712,500
Specified						
Executives						
J Iswaran	250,000		~	-		- 250,000
C Wraight	-		-	1,687,500 (e)		- 1,687,500
G Tachas (c)	250,000		-	-		- 250,000
K Andrews	•		-	-		
N Korchev	=		-	-		-
Total	41,784,999			3,436,539		45,221,538

<sup>(</sup>a) all shares held by entity in which director has a beneficial interest.

#### (f) Transactions and Balances with Related Parties

The following transactions and balances were held with director related entities during the year ended 30 June 2004:

- (i) Dr Stanley Crooke, a director of the company is also a director of Isis Pharmaceuticals Inc ('Isis'). During the year Isis provided various research and development related services to the company. The company paid Isis \$278,740.98 for these services and at year end owes Isis \$303,712.15 for services not invoiced.
- (ii) Professor George Werther, a director of the company is an executive officer of the Murdoch Childrens Research Institute ('MCRI'). During the year the MCRI provided research services in accordance with the Research Agreement entered into between the MCRI and the company. The company paid the MCRI \$334,239.61 for these services of which \$202,846,27 were incurred and expensed as research and development costs. The remaining balance of \$131,393.34 has been treated as a receivable at year end.
- (iii)Payments were made to Metabolic Pharmaceuticals Limited ('Metabolic') during the year as reimbursement for various administrative costs. Dr Chris Belyea, a non-executive director of the company is also the managing director of Metabolic. The total amount paid to Metabolic during the year was \$2,219.33.

<sup>(</sup>b) all shares held by an entity in which director has a beneficial interest.

<sup>(</sup>c) 125,000 shares held by an entity in which specified executive has a beneficial interest.

<sup>(</sup>d) shares acquired from the Murdoch Childrens Research Institute (MCRI) under an option agreement between the MCRI and G Werther.

<sup>(</sup>e) shares acquired from the Murdoch Childrens Research Institute (MCRI) under an option agreement between the MCRI and C Wraight.

	2004	2003
NOTE 17. REMUNERATION OF AUDITORS	\$	\$
Remuneration received, or due and receivable by the auditor for: Amounts received or due and receivable by Ernst & Young Australia for		
- an audit or review of the financial report of the entity - other services in relation to the entity	20,250	19,900
- tax compliance - assurance related	12,323 15,111	15,152 1,500
Total	47,684	36,552
NOTE 18. COMMITMENTS		
(a) Expenditure commitments relating to research and development	are payable as follows:	
Not later than one year  Later than one year and not later than five years	2,425,408 202,287	1,247,678
·	2,627,695	1,247,678
(b) Lease expenditure commitments:		
Not later than one year  Later than one year and not later than five years	190,263 105,129	45,087
	295,392	45,087
NOTE 19. EMPLOYEE BENEFITS		
	2004 \$	2003 \$
(a) Employee benefits Provisions (current) (Note 8)	138,512	38,101

# (b) Employee Option Ownership Scheme

Antisense Therapeutics Limited offers options over ordinary shares to employees at the discretion of the Board of Directors. There are currently four employees eligible to participate in this scheme. Options issued to employees are not listed options and as such do not have a readily available market value.

#### NOTE 19. EMPLOYEE BENEFITS (CONTINUED)

Details of the employee options ownership scheme are as follows:

	2004		2003	
	Number of options	Weighted average exercise price	Number of options	Weighted average exercise price
Balance at beginning of year - granted	5,350,000	0.20	5,350,000	0.20
- exercised	-	-	-	-
- expired	150,000	0.20	-	-
Balance at end of year	5,200,000	0.20	5,350,000	0.20
Exercisable at end of year	3,120,000	0.20	1,070,000	0.20

The following summarises information about options held by employees as at 30 June 2004 \*:

Number of Options	Grant Date	Vesting Dates	Expiry Date	Average Exercise Price
5,200,000	3 December 2001	1 August 2002 - 20%	31 July 2005	\$0.20
		1 August 2003 – 40%		
		1 August 2004 – 40%		

<sup>\*</sup> No options were granted during the year, and no options held by employees as at 1 July 2003 were exercised the year. During the year 150,000 options expired upon the resignation of one employee.

#### NOTE 20. SEGMENT INFORMATION

The company operates in one industry and one geographical segment, those being the pharmaceutical and healthcare industry and Australia respectively.

#### NOTE 21. IMPACT OF ADOPTING AASB EQUIVALENTS TO IASB STANDARDS

Antisense Therapeutics Limited has commenced transitioning its accounting policies and financial reporting from current Australian Standards to Australian equivalents of International Financial Reporting Standards (IFRS). The company has allocated internal resources to identify and assess the key areas that will be impacted by the transition to IFRS. These key areas have been prioritised based on likelihood of material impact. The Board of Directors is overseeing the progress of this transition to IFRS. Expert advice may be sought as required to assist the company in the interpretation of pending AASB's (Australian equivalents of IFRS).

As Antisense Therapeutics Limited has a 30 June year end, priority has been given to considering the preparation of an opening balance sheet in accordance with AASB equivalents to IFRS as at 1 July 2004. This will form the basis of accounting for Australian equivalents of IFRS in the future, and is required when Antisense Therapeutics Limited prepares its first fully IFRS compliant financial report for the year ended 30 June 2006.

Set out below are the key areas where accounting policies will change and may have an impact on the financial report of Antisense Therapeutics Limited. At this stage the company has not been able to reliably quantify the impacts on the financial report.

#### Share Based Payments

Under AASB 3 Share Based Payments, the company will be required to determine the fair value of options issued to employees as remuneration and recognise an expense in the Statement of Financial Performance. This standard is not limited to options and also extends to other forms of equity-based remuneration. It applies to all share-based payments issued after 7 November 2002, which have not vested as at 1 January 2005. Reliable estimation of the future financial effects of this change in accounting policy is impracticable as the details of future equity remuneration plans are unknown. Where future share based payments are issued however, it is likely that expenses will be recognised resulting in reduced profits in future periods.

#### Intangible Assets

Under AASB 138 Intangible Assets, intangible assets that do not meet the standard's recognition criteria are to be "derecognised" from the balance sheet. Once an intangible asset meets the standard's recognition criteria, it will only be subject to amortisation should it be determined to have a finite useful life.

Antisense Therapeutics Limited's intangible asset comprises intellectual property relating to certain rights granted to the company by Isis Pharmaceuticals Inc. and the Murdoch Childrens Research Institute upon listing of the company. Whilst this intangible asset meets the standard's recognition criteria and has been assessed has having a finite useful life, regular assessments of the asset's remaining useful life will need to be conducted to ensure its correct measurement.

# **Directors' Declaration**

In accordance with a resolution of the directors of Antisense Therapeutic Limited, we state that:

- (1) In the opinion of the directors:
  - (a) the financial statements and notes of the company are in accordance with the Corporations Act 2001, including:
    - giving a true and fair view of the company's financial position as at 30 June 2004 and of their performance for the year ended on that date; and
    - (ii) complying with Accounting Standards and Corporations Regulations 2001; and
  - (b) there are reasonable grounds to believe that the company will be able to pay its debts as and when they become due and payable.

On behalf of the Board

Robert W Moses

Chairman

Mark Paul Diamond Managing Director

Melbourne 26 August 2004

# **OTHER INFORMATION**

	2004	2003
NTA backing  Net tangible asset backing per ordinary security	\$0.04	\$0.03
Ratios		
Net loss from ordinary activities after tax attributable to members as a percentage of equity at the end of the year	(26.9%)	(52.6%)
Earnings per share		
Basic earnings per share (cents per share) Diluted earnings per share (cents per share)	(1.37) (1.37)	(2.46) (2.46)

# Status of audit of accounts

This Appendix 4E is based on accounts which have been audited. The audit report is included with the financial report which forms part of this Appendix 4E.

# **Annual General Meeting**

The Annual General Meeting will be held as follows:

Place:

Computershare Conference Centre

Yarra Falls

452 Johnston Street

Abbotsford Victoria 3067 Australia

Date:

20 October 2004

Time:

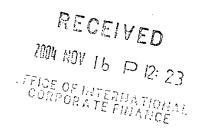
9.30am

Approximate date the annual report will be

available:

20 September 2004





27 September 2004

# ATL1101 for Psoriasis "Proof of Concept" Study - Update

- The Company's current program of toxicology investigations has been completed
- An application for approval to commence the study has been submitted
- On track to commence study Q4, 2004

Antisense Therapeutics has previously advised of its intention to undertake a "proof of concept" study of ATL1101 in patients suffering from Psoriasis.

ATL1101 is a second-generation antisense drug designed to block the synthesis of the IGF-1 receptor, a protein involved in the regulation of cell growth in Psoriasis. The product is being developed as a cream for the treatment of mild to moderate cases of Psoriasis.

The Company recently announced that the manufacture of the active pharmaceutical ingredient and formulation of the cream presentations of ATL1101 for use in the "proof-of-concept" study had been completed.

The Company is now pleased to advise that it has completed its current program of toxicology investigations and has submitted an application for approval to commence the "proof of concept" study with the Institutional Review Board and the relevant Ethics Committee of the Australian Clinical Research Organisation ('CRO') that will conduct the study.

Details of the study, including the CRO which will oversee the running of the trial, will be released once the official approvals to commence the "proof of concept" study have been received. Subject to receiving these approvals the trial is expected to begin on schedule in Q4, 2004.

The Psoriasis project is supported by a Commonwealth Government R&D Start grant of \$1.1 million.

Psoriasis is a chronic, non-contagious skin disorder, which affects 2% of the population. While the precise cause of psoriasis is unknown, it is thought to be triggered by an immune system defect leading to excessive skin cell division. Severity varies, with around 75% of psoriasis cases classified as "mild to moderate", and the remainder classified as "moderate to severe". Topical therapies are first-line treatments for mild to moderate cases of the disease. The worldwide market for psoriasis treatments was more than US\$500 million in 2000 and there is an acknowledged unmet medical need for more effective and safer treatments. The market is forecast to grow to beyond US\$2 billion with the emergence of new therapies.

ATL1101 "Proof of Concept" Study is a double-blind, within-subject randomised, placebocontrolled, proof of concept, comparison study of ATL1101 topical cream in psoriasis patients, using the Microplaque (Small Plaque) Assay.

In this "proof of concept" study a relatively small quantity of ATL1101 will be applied to areas of psoriatic skin on a limited number of patients.

Typically a drug's activity is not established until completion of Phase II clinical trials. However, a "proof of concept" study of ATL1101 can be undertaken relatively inexpensively for a disease such as Psoriasis (unlike for many other diseases), which will provide early evidence of activity. While the "proof of concept" study will not replace the requirement to undertake formal (Phase I, II and III) human clinical trials, if early indications of activity are shown, the company will have increased confidence in the prospects for successful commercial development of ATL1101.

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

Contact Information:

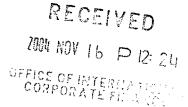
Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999

Street number & name study 1 TOORAK state very 1 TOORAK very 1 T		TISENSE THERAPEUTICS LIMITED		ļ
Season for lodgement of statements and reports   Statements of linearity statements of linearity statements and reports   Statements and reports	*	Prop		1
Australian Securities & Investments Commission  copy of financial statements and reports  ANTISENSE THERAPEUTICS LIMITED  ANTISENSE THERAPEUTICS LIMITED  O 9 5 060 7 45  Reason for lodgement of statements and reports  Usk the appropriate box (3) A public company or a disclosing entity which is not a registered scheme or prescribed interest undertaking (4) A registered scheme of the antique proprietary company that is not a registered scheme or prescribed interest undertaking (5) A registered scheme of financial statements or directors' report (graphany)    A read proprietary company that is not a disclosing entity or a financial statement of financial statements or directors' report (graphany)    A small proprietary company that is not a disclosing entity or a financial statement or directors' report (graphany)    A small proprietary company that is not a disclosing entity or a financial statement or directors' report (graphany)    A small proprietary company that is requested by ASIC to prepare and lodge statements and reports    O   A small proprietary company that is requested by ASIC to prepare and lodge statements and reports    O   A small proprietary company that is requested by ASIC to prepare and lodge statements and reports    O   A small proprietary company that is requested by ASIC to prepare and lodge statements and reports    O   A small proprietary company that is requested by ASIC to prepare and lodge statements and reports    O   A small proprietary company that is not a ediscioning entity please complete the following information as at the entit of the financial year for which the financial statements relate:    A   What is the company is a large proprictary company that is not a discioning entity, please complete the following information as at the entit of the financial year for which the financial statements relate:    A   What is the value of the consolidated gross presenting revenue of the large proprietary company and the entities that it controls?    B   What is the value of the consoli	suburb/city T(			
Australian Securities & Investments Commission  Copy of financial statements and reports    Australian Securities & Investments Commission   24, 28, 28-30, 307, 388, 319, 321, 22   Copyrations Act 2001   24, 28, 28-30, 307, 388, 319, 321, 22   Copyrations Regulations   1,0.88				TASS CORFOAC
Australian Securities & Investments Commission  copy of financial statements and reports  ANTISENSE THERAPEUTICS LIMITED  ANTISENSE THERAPEUTICS LIMITED  O 9 5 060 7 45  Reason for lodgement of statements and reports  Itck the appropriate box A public company or a disclosing entity which is not a registered scheme or prescribed interest undertaking (A) A registered scheme? (B) A registered scheme? (C) A registered scheme? (C) A small propietary company that is not addissing entity or all or part of the period and where the company's profit or spot the period is not covered by the Statements lodged with ASIC by a registered scheme? (D) A small propietary company that is not addissing entity or paper and lodge statements and reports  Dates on which financial spatements undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) A prescribed interest undertaking that is a disclosing entity (D) Bates on which financial spatements and report (D)  What is the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the entit of the manufal year for which the financial statements relate:  A What is the concentration of the consolidated gross persisting reverse of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assess of the large proprietary company and the entities that it controls?  C How many members does the large proprietary company have?  B What is the value of the consolidated gross assess of the large proprietary company and the entities that it co	<u>· · ·</u>			CASH. REQ.P
Copy of financial statements and reports  Copy of financial statements and reports  Name  ANTISENSE THERAPEUTICS LIMITED  O95 060 745  Reason for lodgement of statements and reports  tick the appropriate box A public company or a disclosing entity which is not a registered scheme or prescribed interest undertaking  (A)  Amendment of financial statements or director's report (company)  A small proprietary company that is not acclosing entity  A small proprietary company that is required by ASIC to prepare and lodge statements and reports  U)  A small proprietary company that is required by ASIC to prepare and lodge statements and reports  U)  Cutes on which financial syrae begins  1 /7 / 2003  and ends  3 0 / 6 / 2004  (d/m/y)  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the value of the consolidated gross assess of the large proprietary company and the entities that it controls?  Level the financial statements audited? Yes \( \omegains \) No  Were the financial statements audited? Yes \( \omegains \) No  No see the auditor's report (section 309) for the financial year contain a statement ob-  * reasons for the auditor not being satisfied as to the muters referred to in section 3077 Yes \( \omegains \) No  Bedieter of the section 3077 Yes \( \omegains \) No  * details of the detellingent, failar of shortcoming any matter referred to in section 3077 Yes \( \omegains \) No  * details of the detellingent, failar of shortcomin	DX number	suburb/city TFICE OF INTERNAL L		PROC
Copy of financial statements and reports  Copy of financial statements and reports  Name  ANTISENSE THERAPEUTICS LIMITED  O95 060 745  Reason for lodgement of statements and reports  tick the appropriate box A public company or a disclosing entity which is not a registered scheme or prescribed interest undertaking  (A)  Amendment of financial statements or director's report (company)  A small proprietary company that is not acclosing entity  A small proprietary company that is required by ASIC to prepare and lodge statements and reports  U)  A small proprietary company that is required by ASIC to prepare and lodge statements and reports  U)  Cutes on which financial syrae begins  1 /7 / 2003  and ends  3 0 / 6 / 2004  (d/m/y)  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the value of the consolidated gross assess of the large proprietary company and the entities that it controls?  Level the financial statements audited? Yes \( \omegains \) No  Were the financial statements audited? Yes \( \omegains \) No  No see the auditor's report (section 309) for the financial year contain a statement ob-  * reasons for the auditor not being satisfied as to the muters referred to in section 3077 Yes \( \omegains \) No  Bedieter of the section 3077 Yes \( \omegains \) No  * details of the detellingent, failar of shortcoming any matter referred to in section 3077 Yes \( \omegains \) No  * details of the detellingent, failar of shortcomin	<u> </u>	WAT URATE FOR THE	200	
Copy of financial statements and reports   Copy and Cop	Aus	tralian Securities & Investments Commission		
Name ACN / ARBN / ARSN/PN    ANTISENSE THERAPEUTICS LIMITED   095 060 745			•	i i
Name   ACN / ARSN / ARSN/PIN   ASSN/PIN   O.9.5 0.6.0 7.4.5	<b>₩</b> C0	py of financial statements and reports		,
Name   ACN / ARBN / ARSN/PN   O.9.5 0.6.0 74.5				ons
Reason for Iodgement of statements and reports			1.0.00	
Reason for Iodgement of statements and reports	Name ·	NULT CONTO DIVERNA DELIBERA E TALEBON		
Reason for lodgement of statements and reports    tick the appropriate box   A public company or a disclosing entity which is not a registered scheme or prescribed interest undertaking   (A)   A registered scheme*   (B)   A registered scheme*   (B)   A mendment of financial statements or directors' report (registered scheme)*   (C)   A large proprietary company that is not a disclosing entity   (P)   A small proprietary company that is not a disclosing entity   (P)   A small proprietary company that is controlled by a foreign company for all or part of the period and where the company's profit relies for the period is not covered by the statements lodged with ASIC by a registered foreign company, company, company, registered scheme, or disclosing entity   (P)   A small proprietary company that is requested by ASIC to prepare and lodge statements and reports   (D)   A prescribed interest undertaking that is a disclosing entity   (P)	·		<del></del>	
tick the appropriate box A public company or a disclosing entity which is not a registered scheme or prescribed interest undertaking (A) A registered scheme* (B) A mendment of financial statements or directors' report (registered scheme)* (C) A mendment of financial statements or directors' report (registered scheme)* (D) A farge proprietary company that is not a disclosing entity (P) A small proprietary company that is not a disclosing entity of the period and where the company's profit or loss for the period is not covered by the statements lodged with ASIC by a registered foreign company; company, registered scheme, or disclosing entity (R) A small proprietary company that is requested by ASIC to prepare and lodge statements and reports (P) A prescribed interest undertaking that is a disclosing entity (R) Details of large proprietary company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  Auditor report  Were the financial statements audited? Yes x: No   Yes Des the auditor's report (section 308) for the financial year contain a statement of:  * reasons for the auditor not being statisfied as to the matters referred to in section 3077 Yes   * details of the deficiency, failure or shortcorning any matter referred to in section 3077 Yes   No   * details of the deficiency, failure or shortcorning any matter referred to in section 3077 Yes   No   * details of the deficiency, failure or shortcorning any matter referred to in section 3077 Yes	7.017 7.1017 7.1017 111	095 060 745		
tick the appropriate box A public company or a disclosing entity which is not a registered scheme or prescribed interest undertaking (A) A registered scheme* (B) A mendment of financial statements or directors' report (registered scheme)* (C) A mendment of financial statements or directors' report (registered scheme)* (D) A farge proprietary company that is not a disclosing entity (P) A small proprietary company that is not a disclosing entity of the period and where the company's profit or loss for the period is not covered by the statements lodged with ASIC by a registered foreign company; company, registered scheme, or disclosing entity (R) A small proprietary company that is requested by ASIC to prepare and lodge statements and reports (P) A prescribed interest undertaking that is a disclosing entity (R) Details of large proprietary company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  Auditor report  Were the financial statements audited? Yes x: No   Yes Des the auditor's report (section 308) for the financial year contain a statement of:  * reasons for the auditor not being statisfied as to the matters referred to in section 3077 Yes   * details of the deficiency, failure or shortcorning any matter referred to in section 3077 Yes   No   * details of the deficiency, failure or shortcorning any matter referred to in section 3077 Yes   No   * details of the deficiency, failure or shortcorning any matter referred to in section 3077 Yes				1
A registered scheme* A registered scheme* A registered scheme* A mendment of financial statements or directors' report (company) A hard for financial statements or directors' report (registered scheme)*  A large proprietary company that is not a disclosing entity A small proprietary company that is not not covered by the statements lodged with ASIC by a registered foreign company, company, company, registered scheme, or disclosing entity  A small proprietary company that is requested by ASIC to prepare and lodge statements and reports  U) A prescribed interest undertaking that is a disclosing entity  No Dates on which financial year begins  1/7 / 2003 and ends 30 / 6 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?	Reason for loagement of s	tatements and reports		
A registered scheme* A registered scheme* A registered scheme* A mendment of financial statements or directors' report (company) A hard for financial statements or directors' report (registered scheme)*  A large proprietary company that is not a disclosing entity A small proprietary company that is not not covered by the statements lodged with ASIC by a registered foreign company, company, company, registered scheme, or disclosing entity  A small proprietary company that is requested by ASIC to prepare and lodge statements and reports  U) A prescribed interest undertaking that is a disclosing entity  No Dates on which financial year begins  1/7 / 2003 and ends 30 / 6 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?	tick the appropriate boy 🕏	A public company or a disclosing antity which is not a registered schome or process	rihad interact undertaking	(Δ)
Amendment of financial statements or directors' report (company)  Amendment of financial statements or directors' report (registered scheme)*  A large proprietary company that is not a disclosing entity  A small proprietary company that is controlled by a foreign company for all or part of the period and where the company's profit or loss for the period is not covered by the statements lodged with ASIC by a registered foreign company, company, registered scheme, or disclosing entity  A small proprietary company that is requested by ASIC to prepare and lodge statements and reports  U)  A prescribed interest undertaking that is a disclosing entity  Bates on which financial year begins  1 /7 / 2003 and ends  3 0 / 6 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?  1 yes: Does the auditor's report (section 308) for the financial year contain a statement of:  * reasons for the auditor on to being satisfied as to the matters referred to in section 307? Yes   No   No   No   No   No   No   No   N			nibed interest undertaking	
Amendment of financial statements or directors' report (registered scheme)*    A starge proprietary company that is not a disclosing entity   A small proprietary company that is not a disclosing entity   A small proprietary company that is not overed by the statements lodged with ASIC by a registered foreign company, company, registered scheme, or disclosing entity   O small proprietary company that is requested by ASIC to prepare and lodge statements and reports   O small proprietary company that is requested by ASIC to prepare and lodge statements and reports   O small proprietary company that is requested by ASIC to prepare and lodge statements and reports   O small proprietary company that is requested by ASIC to prepare and lodge statements and reports   O states on which financial year begins	Ä	-		
A small proprietary company that is controlled by a foreign company for all or part of the period and where the company's profit or loss for the period is not covered by the statements lodged with ASIC by a registered foreign company, registered scheme, or disclosing entity (I)  A small proprietary company that is requested by ASIC to prepare and lodge statements and reports (J)  A prescribed interest undertaking that is a disclosing entity (K)  Dates on which financial year begins 1 /7 / 2003 and ends 30 / 6 / 2004 (d/m/y)  Date of Annual General Meeting (if applicable) 20 / 10 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?  D How many members does the large proprietary company have?  If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  1 reasons for the auditor not being satisfied as to the matters referred to in section 307?  2 details of the deficiency, failure or shortcoming concerning any matter referred to in section 307?  3 No S	$\Box$	· · · · · · · · · · · · · · · · · · ·		
company's profit or loss for the period is not covered by the statements lodged with ASIC by a registered foreign company, company, company, registered scheme, or disclosing entity ()  A small proprietary company that is requested by ASIC to prepare and lodge statements and reports (J)  A prescribed interest undertaking that is a disclosing entity (K)  Dates on which financial year begins 1 /7 / 2003 and ends 30 / 6 / 2004 (d/m/y)  Date of Annual General Meeting (if applicable) 20 / 1.0 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?		A large proprietary company that is not a disclosing entity		(H)
company, company, registered scheme, or disclosing entity (1)  A small proprietary company that is requested by ASIC to prepare and lodge statements and reports (J)  A prescribed interest undertaking that is a disclosing entity (K)  Dates on which financial year begins 1/7 / 2003 and ends 30 / 6 / 2004 (U/m/y)  Date of Annual General Meeting (if applicable) 20 / 10 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?		A small proprietary company that is controlled by a foreign company for all or part	of the period and where the	
A small proprietary company that is requested by ASIC to prepare and lodge statements and reports  A prescribed interest undertaking that is a disclosing entity  Dates on which financial year begins  1 /7 / 2003 and ends  30 / 6 / 2004  (d/m/y)  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?		company's profit or loss for the period is not covered by the statements lodged with	th ASIC by a registered foreign	
Dates on which financial year begins  1 /7 / 2003 and ends 30 / 6 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?				
Dates on which financial year begins 1/7 / 2003 and ends 30 / 6 / 2004 (d/m/y)  Date of Annual General Meeting (if applicable) 20 / 10 / 2004  Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?	Ļ		ments and reports	
Details of large proprietary company  If the company is a large proprietary company that is not a disclosing entity, please complete the following information as at the end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?	Ļ	A prescribed interest undertaking that is a disclosing entity		(K)
end of the financial year for which the financial statements relate:  A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?				
A What is the consolidated gross operating revenue of the large proprietary company and the entities that it controls?  B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?			omplete the following informati	on as at the
B What is the value of the consolidated gross assets of the large proprietary company and the entities that it controls?  C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?		•	d the exitition that it controls?	
C How many employees are employed by the large proprietary company and the entities that it controls?  D How many members does the large proprietary company have?		nat is the consolidated gross operating revenue of the large proprietary company an	a me entities mar it comons:	
Auditor report  Were the financial statements audited? Yes No   If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307? Yes No  • details of the deficiency, failure or shortcoming concerning any matter referred to in section 307? Yes No	B W	hat is the value of the consolidated gross assets of the large proprietary company a	nd the entities that it controls?	
Auditor report  Were the financial statements audited? Yes No   If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307? Yes No  • details of the deficiency, failure or shortcoming concerning any matter referred to in section 307? Yes No	Γ			
Auditor report  Were the financial statements audited? Yes No  No  If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307? Yes  No  Average  No  Average  No  Average  No  No  Average  No  Average  No  No  No  Average  No  No  No  Average  No  No  No  No  No  No  No  No  No  N	C Ho	w many employees are employed by the large proprietary company and the entities	that it controls?	
Auditor report  Were the financial statements audited? Yes No  No  If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307? Yes  No  Average  No  Average  No  Average  No  No  Average  No  Average  No  No  No  Average  No  No  No  Average  No  No  No  No  No  No  No  No  No  N	Ĺ		•	•
Auditor report  Were the financial statements audited? Yes No  No  If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307? Yes  No  Average  No  Average  No  Average  No  No  Average  No  Average  No  No  No  Average  No  No  No  Average  No  No  No  No  No  No  No  No  No  N	ת של	www.manu.mambare.doos the large preprietany.company.hous?		
Were the financial statements audited? Yes \( \sqrt{1}\) No \( \)  If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307? Yes \( \) No \( \sqrt{2}\) • details of the deficiency, failure or shortcoming concerning any matter referred to in section 307? Yes \( \) No \( \sqrt{2}\)	D III	w many members does die large proprietary company naver		
Were the financial statements audited? Yes \( \sqrt{1}\) No \( \)  If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307? Yes \( \) No \( \sqrt{2}\) • details of the deficiency, failure or shortcoming concerning any matter referred to in section 307? Yes \( \) No \( \sqrt{2}\)				
If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307?  • details of the deficiency, failure or shortcoming concerning any matter referred to in section 307?  • Yes  No  \overline{\text{X}}	Auditor report			
If yes: Does the auditor's report (section 308) for the financial year contain a statement of:  • reasons for the auditor not being satisfied as to the matters referred to in section 307?  • details of the deficiency, failure or shortcoming concerning any matter referred to in section 307?  • Yes  No  \overline{\text{X}}				
reasons for the auditor not being satisfied as to the matters referred to in section 307?  Yes No   details of the deficiency, failure or shortcoming concerning any matter referred to in section 307?  Yes No   No		<del></del> -		
* details of the deficiency, failure or shortcoming concerning any matter referred to in section 307? Yes 🔲 No 🗵	If yes: Do	·		u. 🗊
			_	=
The state of the s	If no. Is			
	n 110. 13	and a disast order exemption earters for audit tener.	,,,,	ب ٠٠٠
·				
<ul> <li>NOTE: Where a new auditor has been appointed to a Registered Scheme, Form 5137 - Appointment of Scheme Auditor must be lodged</li> </ul>				

<b>Details of current audito</b>	r* .		
•	The auditor can be a person or a firm.		
If a person			
name (family & given names)		•	
Auditor Registration no:			
-	office	level	building name
street number & name			
suburb / city	sta	ate / territory	postcode
date of appointment (d/m/y)	/ /	<u> </u>	
or		•	
If a firm			
name of firm	ERNST & YOUNG		
-	office	level 23	building name
street number & name	120 COLLINS STREET	23	
suburb / city		ate / territory VIC	postcode 3000
Business Registration number	tre at the same	· 110	ory registered in VICTORIA
date of appointment (d/m/y)	<u></u>	otato / rome	W) Togisted III VICTORIA
	9 1 2002		· · · · · · · · · · · · · · · · · · ·
Statements and reports	to be attached to this form  Financial statements for the year (as per ss295(2))		
	statement of financial performance for the year (p	rofit and loss statement)	
	statement of financial position as at the end of th	e year (balance sheet)	
	statement of cash flows for the year		
	if required by accounting standards - consolidated	profit & loss statement, balance s	heet and statement of cash flows
	Notes to financial statements (as per ss295(3))		
	disclosures required by the regulations		
	notes required by the accounting standards		
	any other information necessary to give a true and	d fair view (see s297)	
	The directors' declaration should the statements	-d mater (- m - m - 205/4))	
	The directors' declaration about the statements a	iu notes (as per 55 295(4))	
	The directors' report for the year (as per s 298 to	300)	
	Auditor's report required under sections 308 and	314	
Certification	ı		
Certification	I certify that the attached documents marked (	) are a true copy of the annual re	eports required under Section 319.
print name	NATALIE KORCHEV	capacity	COMPANY SECRETARY
sign here	N. Korchel	date	28/9/04
-			
• NOTE:	Where a new auditor has been appointed to a Re	egistered Scheme, Form 5137 - Ap	pointment of Scheme Auditor must be lodged
	Small Business (less than 20 employees), please Include The time actually spent reading the inst The time spent by all employees in colle	ructions, working on the question a	ind obtaining the information





6 October 2004

### Antisense Therapeutics to establish Level 1 American Depository Receipt Program

Antisense Therapeutics is pleased to announce that it has accepted a proposal from The Bank of New York to establish a Level 1 American Depository Receipt (ADR) program.

The establishment of this ADR program will facilitate the purchase of Antisense Therapeutics shares by United States investors.

This initiative is a logical extension of the Company's focus on its international development, and an appropriate vehicle to leverage the high awareness of and regard for antisense technology generally and the growing international interest in Antisense Therapeutics' product development plans specifically.

Mark Diamond, CEO of Antisense commented: "We are very excited to take this initial step in bringing the Antisense story to international investors. A vital part of our long-term strategy to enhance shareholder value is to improve liquidity and broaden and diversify our shareholder base by enhancing the Company's visibility in the world's largest capital market. The ADR program will help us capitalize on landmark achievements by making investing easier for existing and potential US investors."

### About ADRs

ADRs are commonly used to facilitate US investors investing in foreign companies not listed in the USA. An ADR is created when a broker purchases a company's shares on the home stock market and delivers those to the depositary's local custodian bank, which then instructs the depositary bank, The Bank of New York, to issue Depositary Receipts. Depositary receipts may trade freely, just like any other security, in the over-the-counter (OTC) market.

### About Antisense Therapeutics Limited

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS) and Queensland Investment Corporation.

Contact Information:

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999



20 October 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

### Results of Annual General Meeting: 20 October 2004

As required by section 251AA(2) of the Corporations Act and ASX Listing Rule 3.13.2, the following statistics are provided in respect to each motion set out in the company's Notice of Annual General Meeting, which was lodged with the ASX on 21 September 2004.

In respect to each motion the total number of votes exercisable by all validly appointed proxies was:

### Re-election of Director - Mr Robert Moses

ū	Votes where the proxy directed to vote 'for' the motion	218,492,306
	Votes where the proxy was directed to vote 'against' the motion	20,000
	Votes where the proxy may exercise a discretion how to vote:	
	o Chairman	2,374,342
	o Other	48,240
In a	addition, the number of votes where the proxy was directed to abstain from voting on	
the	e motion was	184,500

The motion was carried on a show of hands as an ordinary resolution.

### Re-election of Director - Professor Graham Mitchell

	Votes where the proxy directed to vote 'for' the motion	218,063,306
	Votes where the proxy was directed to vote 'against' the motion	25,000
	Votes where the proxy may exercise a discretion how to vote:	
	o Chairman	2,414,342
	o Other	48,240
In a	addition, the number of votes where the proxy was directed to abstain from voting on	
the	e motion was	568,500

The motion was carried on a show of hands as an ordinary resolution.

Yours faithfully

Natalie Korchev Company Secretary





20 October 2004

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam

Re: Annual General Meeting 2004 - Presentation

Please find enclosed the Chairman's address to shareholders and the presentation to be made by the Managing Director this morning at Antisense Therapeutics Limited's Annual General Meeting.

Yours sincerely

Natalie Korchev Company Secretary

### ANTISENSE THERAPEUTICS LIMITED CHAIRMAN'S ADDRESS ANNUAL GENERAL MEETING 20 October 2004

Ladies and Gentlemen, welcome to this 3<sup>rd</sup> Annual General Meeting of the members of Antisense Therapeutics Limited.

I would like to introduce the directors and company secretary of the Company Dr Chris Belyea
Dr George Werther
Prof Graham Mitchell
Mr Mark Diamond, CEO
Dr Stanley Crooke, who is in the US and could not attend the meeting; and Natalie Korchev our Company Secretary

Antisense Therapeutics has had a productive and successful year achieving a number of important development milestones, in a timely manner and on budget:

- The Company's lead compound for the treatment of multiple sclerosis, ATL1102, completed Phase I human trials in healthy volunteers. This is essentially a safety trial. Preparations are now nearly complete for the Phase IIa trial which Mark Diamond will discuss in more detail at the conclusion of the official business of the meeting.
- The company's second lead compound is ATL1101 for psoriasis. The company is planning to undertake a 'proof-of-concept' study in patients with psoriasis which Mark Diamond will also speak to in more detail during his presentation.
- Another major development has been the encouraging flow of new antisense projects from our Discovery & Research team, the most advanced project being our antisense inhibitor to the growth hormone receptor which offers the prospect of treating a disease called acromegaly and diabetic retinopathy.

At the conclusion of the official business of the meeting this morning our Managing Director, Mark Diamond, will provide you with a summary of all of the Company's achievements during the financial year just completed and offer some insights with respect to plans going forward.

Before moving to the business of the meeting I would like to offer a few observations with respect to the Antisense share price and the Company's operating performance. A number of Australia's best market analysts have over the past year produced quite favourable reports about Antisense Therapeutics Limited, but the Company's share price has languished, and in my view has been a considerable disappointment. Typical of analysts comments is this one, quote: "Antisense Therapeutics – variable share price performance but great operational progress". I would certainly agree with the great progress, but be inclined to say "disappointing share price performance but great operational progress". In my view, the Antisense management team has performed admirably, has achieved essentially all of the key objectives set out for it at the beginning of the year, and has delivered real and encouraging results. Unfortunately the share price has drifted in a flat to downward direction, apparently not attributing anything at all to the underlying value creation.

By any measure I know, Antisense Therapeutics is fundamentally a more valuable company today than it was a year ago, but this is not reflected in the share price. In my view this "disconnect" between the share price and the real value of the Company is primarily a function of short term trading and thin trading volumes. This "disconnect" phenomenon seems to be endemic within the Australian biotech sector, but it is a reality we must address.

Good biotechnology companies like Antisense Therapeutics offer <u>long term investors</u> the prospect of obtaining exponential capital appreciation, however in the immediate past, and probably in the immediate future, it is the short term traders which tend to exert the most influence on share price, particularly during periods of thin trading volume.

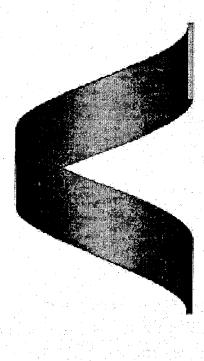
This "disconnect" between share price and intrinsic value of the Company is frustrating to your board and management and I'm sure also to our loyal long term shareholders. There are however, a few things we can do, will do and are doing to address this problem.

First, and foremost we will continue to build market credibility by remaining tenaciously focussed on achieving objectives and results and by promoting the quality and commercial value of the Company's product pipeline.

Second, our strategy and decision-making must remain dedicated to long term value creation. We must not yield to the pressures to announce something every month or two if it is not genuinely of material importance to shareholders. Frequent market announcements without substance may generate a bit of trading activity, but over time will destroy credibility and more than likely contribute to erosion in share price. However, we need to continue to, on a regular basis, provide updates and explanations about the Company so that influential participants in the capital markets can understand and appreciate the intrinsic value of Antisense Therapeutics Limited.

Third, we must explore all opportunities to strengthen and broaden the share register by attracting more genuine long term investment. Initiatives to consider include: a) enhancing liquidity for northern hemisphere investors; b) structuring commercial agreements to include risk sharing or perhaps even an equity component; and c) possibly merger or acquisition to build critical mass, as well as financial and technical strength.

Realistically, none of these initiatives is likely to cause an overnight re-rating of the Company's share price, but in time I am confident that our share price can be "re-connected" to the real value of the Company particularly as the company moves into patient trials on its lead compounds and pivotal data emerges from these studies, and when this happens, our long term investors should hopefully be handsomely rewarded.



# ANTISENSE THERAPEUTICS

Annual General Meeting

## **Overview**

- Corporate Structure
- Mission/Strategy
- Key Achievements
- Lead Projects
- Outlook
- Summary



Total funds raised to date: \$28.5 M

Market Capitalisation: A\$41M (undiluted)

Key Shareholders

- Circadian 20%

15% (42% Circadian)

- Syngene

- Isis

11%

- <u>QC</u>

2%

Cash reserves of \$12M, no borrowings



## **ANP's Mission**

pharmaceuticals for large and/or niche unmet markets Create, develop and commercialize novel antisense

Select targets where our technology will provide clear competitive advantages



# **Business Strategy**

- Leverage 14 years of Isis antisense technology development
- Fast track existing lead projects through pre-clinical and clinical development
- Create pipeline of new antisense therapeutics
- Commercialise those that are successful in clinical testing via licensing/partnering



# Key Achievements - FY to 30 June 2004

## ATL1102 for MS

successfully completed Phase I human clinical trial

# ATL1101 for Psoriasis

- completed animal toxicology study for "Proof of Concept" study
- filed application for "Proof of Concept" study

# ATL1103 for Growth and Sight Disorders

new development project

Capital Raising - A\$10.4M

# Level 1 ADR program

Accepted proposal from Bank of New York



# Development Progress 2002 - 2004

## Dec 2001

## Q4 2004

ATL1102 MS	Pre-clinical efficacy in animals	Scheduled to start Phase Ila trial in MS patients
ATL1101 Psoriasis	Target validation in animal model	Scheduled to start Proof of Concept trial in patients
ATL1103 Growth and sight disorders	N/A	Completed animal efficacy and selected human lead

"Lead compounds from animal experiments into clinical trials in patients in 3 years"



# Disease & Market

- Life-long chronic disease of the central nervous system
- Global drug sales of > US\$2.5bn in 2002
- Need for more effective drug with less side effects

### **Product**

- Antisense inhibitor to VLA-4 protein
- (also other inflammatory disorders asthma & arthritis) Confirmed activity in pre-clinical mouse model of MS



# VLA-4 is a validated target

Biogen Idec's Antegren™ (also targets VLA-4) is in Phase III

- Marketing application filed with FDA based on interim 1 year phase III data
- Provides greater confidence in likelihood of clinical success of ATL1102
- Anticipate efficacy, dosing and cost advantages with ATL1102



# Biogen Idec climbs on drug's promise

Last Update: 1:38 PM ET Oct. 11, 2004 By Laura Gilcrest, CBS MarketWatch

bigger chunk of the multiple sclerosis market it already dominates. Monday trading as the company stands poised to capture an even WASHINGTON (CBS.MW) -- Shares of Blogen Idec got a boost in

NATURE BIOTECHNOLOGY VOLUME 22 NUMBER 8 AUGUST 2004

## Fast track to MS drug

blockbuster drug as some analysts predict? Cormac Sherican Will the new multiple sclendsis of ug Antegran be the next investigates.

## Elan's Antegren Sales Could Soar 09.08.04, 12:23 PM ET

Antegren by the end of November and the company remains people ) to receive approval for its multiple sclerosis drug Morgan Stanley said it expects Elan (nyse: ELN - news its top pick in the specialty pharmaceuticals sector. "We



## Progress

Completed Phase I human trial

## Outlook

- Preparing an application to conduct a Phase IIa clinical
  - Trial to be conducted in Europe
- Regulatory Agency approval and commencement of trial



# Psoriasis Treatment – ATL1101

# Disease & Market

- Chronic non-contagious skin disorder
- Affects 1-2% of population
- Global drug sales forecast to exceed US\$2 billion by 2007 (Frost & Sullivan)
- Need for more effective therapies

### **Product**

- Antisense inhibitor to IGF-1R; regulates cell growth
- Developing topical formulation

# Psoriasis Treatment – ATL1101

## Progress

- Completed current toxicology program for "Proof of Concept" study
- Submitted application to conduct "Proof of Concept" study
- Awarded A\$1.1 million government grant

### Outlook

 Commence "Proof of Concept" study in psoriasis patients in 2004



# ATL1103 for growth & sight disorders

### **Product**

- Antisense inhibitor to the GH receptor
- GH action is mediated through IGF-1 hormone
- Acromegalics have elevated levels of both GH and IGF-1
- Current acromegaly treatment involves normalising IGF-I levels
- Reduction of IGF-I levels is associated with clinical improvement in retinopathy



# ATL1103 for growth & sight disorders

# Results of Animal Studies

- (existing treatment for acromegaly) in an equivalent mouse IGF-1 suppression by ATL1103 comparable to Trovert<sup>TM</sup> model
- Data presented at 2nd International Symposium on GH & IGF-I, Cairns, Australia, April 2004
- Patent applications filed



# ATL1103 for growth & sight disorders

## **Progress**

Lead compound selected for clinical development

### Outlook

 Place order for bulk drug product to commence preclinical safety studies



## Outlook

Droioct	Value Driver / Milestone	Timing
riojeci	Value Dilvel / Milestolle	8
ATL1102	·Complete Phase I	1st half '04 √
MS	Start Phase IIa	2nd half '04
	<ul> <li>Partnering objective</li> </ul>	Concl Ph Ila
ATL1101 Psoriasis	<ul> <li>Complete product manufacture and toxicology program for "PoC"</li> </ul>	1st half '04 √
	<ul><li>Start "Proof of Concept" study</li></ul>	2nd half '04
	•Partnering objective	Concl "PoC"
ATL1103 Acromegaly	•Commence product manufacture for pre-clinical toxicology (lead selection)	1st half '04 √
	Order compound for pre-clinical toxicology	2 <sup>nd</sup> half '04

### œ

# **ANP – Investment Fundamentals**

# Attractive product pipeline

- Validated targets (lower development risk)
- Products with platform based competitive advantages
- Significant market potential

# Track record for hitting development milestones

- · Mature, efficient, and predictable platform technology
- High quality and effective collaborations (Isis)
- Experienced management team

# Clear commercialisation objectives

# Near term key value drivers







### Antisense Therapeutics to Present at Rodman & Renshaw 6<sup>th</sup> Annual Healthcare Conference

Melbourne, Australia – October 21, 2004 – Antisense Therapeutics Limited (ASX: ANP) today announced that company management will present at the Rodman & Renshaw 6<sup>th</sup> Annual Healthcare Conference at The Waldorf-Astoria Hotel in New York City on Wednesday, October 27, 2004 at 11:50 AM ET.

Mark Diamond, chief executive officer, is scheduled to present to an audience of analysts and portfolio managers. His presentation will include both a company presentation and a moderated discussion between management and institutional investors.

To arrange a one-on-one meeting with Mr. Diamond during the conference, please contact Rachel Levine at The Anne McBride Company, tel. 212-983-1702, ext. 207, or rlevine@annemcbride.com.

### **About Antisense Therapeutics Limited**

Antisense Therapeutics Limited (ASX: ANP) is an Australian publicly listed biopharmaceutical drug discovery and development company. ANP's mission is to create, develop and commercialise novel antisense pharmaceuticals for large unmet markets. Its two most advanced projects target Multiple Sclerosis (ATL1102), and Psoriasis (ATL1101).

ANP plans to commercialise its pipeline via licensing/collaboration agreements with major biotechnology and pharmaceutical companies.

ANP's major shareholders include Circadian Technologies Limited (ASX: CIR), Isis Pharmaceuticals Inc (NASDAQ: ISIS) and Queensland Investment Corporation.

**Contact Information:** 

Website: www.antisense.com.au

Managing Director – Mark Diamond +61 3 9827 8999 Company Secretary – Natalie Korchev +61 3 9827 8999

Rachel Levine - The Anne McBride Co. - 212-983-1702 ext. 207

2004 NOV 15 P 12: CH

OSFICE OF HITERNATUS CORPORATE Appendix 3B

Rule 2.7, 3.10.3, 3.10.4, 3.10.5

### New issue announcement, application for quotation of additional securities and agreement

Information or documents not available now must be given to ASX as soon as available. Information and documents given to ASX become ASX's property and may be made public.

Introduced 1/7/96. Origin: Appendix 5. Amended 1/7/98, 1/9/99, 1/7/2000, 30/9/2001, 11/3/2002, 1/1/2003.

ABN		
41 0	95 060 745	
We (	(the entity) give ASX the following i	nformation.
	rt 1 - All issues nust complete the relevant sections (attach si	heets if there is not enough space).
1	<sup>+</sup> Class of <sup>+</sup> securities issued or to be issued	Ordinary Shares
2	Number of *securities issued or to be issued (if known) or maximum number which may be issued	140
3	Principal terms of the *securities (eg, if options, exercise price and expiry date; if partly paid *securities, the amount outstanding and due dates for payment; if *convertible securities, the conversion price and dates for conversion)	Exercise of 140 ANPO options at 20 cents each to purchase 140 ordinary shares in ANP.

Name of entity

<sup>+</sup> See chapter 19 for defined terms.

4	Do the *securities rank equally in all respects from the date of allotment with an existing *class of quoted *securities?	Yes	
	If the additional securities do not rank equally, please state:  the date from which they do  the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment  the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment	N/A	
5	Issue price or consideration	20 cents per share.	
	process of constant and the constant and		
6	Purpose of the issue (If issued as consideration for the acquisition of assets, clearly identify those assets)	Exercise of 140 ANPO ordinary shares in ANP.	
7	Dates of entering *securities into uncertificated holdings or despatch of certificates	4 October 2004	
•		Number	+Class
8	Number and *class of all *securities quoted on ASX (including the securities in clause 2 if applicable)	355,258,390 91,462,725	Ordinary shares (ANP) Options (ANPO)

<sup>+</sup> See chapter 19 for defined terms.

+Class Number Number and +class of all 11,500,000 Options expiring 31 July +securities not quoted on ASX 2005 exercisable at 20 cents each (ANPAM) (including the securities in clause 2 if applicable) 20,000,000 Options expiring 30 November 2006 exercisable at 20 cents each (ANPAO). Options expiring 31 July 2,200,000 2005 exercisable at 20 cents each (ANPAQ) 10 Dividend policy (in the case of a N/A trust, distribution policy) on the increased capital (interests) Part 2 - Bonus issue or pro rata issue security holder approval N/A required? 12 Is the issue renounceable or non-N/A renounceable? Ratio in which the \*securities will N/A 13 be offered 14 +Class of +securities to which the N/A offer relates 15 +Record date determine N/A to entitlements 16 Will holdings on different registers (or subregisters) be aggregated for calculating entitlements? Policy for deciding entitlements in N/A 17 relation to fractions Names of countries in which the entity has \*security holders who will not be sent new issue documents Note: Security holders must be told how their entitlements are to be dealt with. Cross reference: rule 7.7. Closing date for receipt of N/A acceptances or renunciations

<sup>+</sup> See chapter 19 for defined terms.

20	Names of any underwriters	N/A
21	Amount of any underwriting fee or commission	N/A
22	Names of any brokers to the issue	N/A
23	Fee or commission payable to the broker to the issue	N/A
24	Amount of any handling fee payable to brokers who lodge acceptances or renunciations on behalf of *security holders	N/A
25	If the issue is contingent on *security holders' approval, the date of the meeting	N/A
26	Date entitlement and acceptance form and prospectus or Product Disclosure Statement will be sent to persons entitled	N/A
27	If the entity has issued options, and the terms entitle option holders to participate on exercise, the date on which notices will be sent to option holders	N/A
28	Date rights trading will begin (if applicable)	N/A
29	Date rights trading will end (if applicable)	N/A
30	How do *security holders sell their entitlements in full through a broker?	N/A
31	How do *security holders sell part of their entitlements through a broker and accept for the balance?	N/A

Appendix 3B Page 4

<sup>+</sup> See chapter 19 for defined terms.

32	How do *security holders dispose of their entitlements (except by sale through a broker)?	N/A
33	<sup>+</sup> Despatch date	N/A
	ct 3 - Quotation of secur	
34	Type of securities (tick one)	
(a)	Securities described in Part 1	
(b)	All other securities	
		of the escrowed period, partly paid securities that become fully paid, employee ends, securities issued on expiry or conversion of convertible securities
Ent	ities that have ticked box 34(	a)
Add	itional securities forming a new cla	ass of securities
	_	33 01 300111103
Tick docur	to indicate you are providing the informa	
	to indicate you are providing the informa nents  If the *securities are *equity	
docur	If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity additional *equity	tion or securities, the names of the 20 largest holders of the
docur 35	If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity *securities setting out the number 1 - 1,000 1,001 - 5,000 5,001 - 10,000 10,001 - 100,000	v securities, the names of the 20 largest holders of the enumber and percentage of additional *securities held by the securities, a distribution schedule of the additional aber of holders in the categories
35 36	If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity securities are *equity securities setting out the number 1 - 1,000 1,001 - 5,000 5,001 - 10,000 10,001 - 100,000 100,001 and over	v securities, the names of the 20 largest holders of the enumber and percentage of additional *securities held by the securities, a distribution schedule of the additional aber of holders in the categories
35 36	If the *securities are *equity additional *securities, and the those holders  If the *securities are *equity securities are *equity securities setting out the number 1 - 1,000 1,001 - 5,000 5,001 - 10,000 10,001 - 100,000 100,001 and over	v securities, the names of the 20 largest holders of the enumber and percentage of additional *securities held by the securities, a distribution schedule of the additional aber of holders in the categories

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

### Entities that have ticked box 34(b)

38	Number of securities <sup>†</sup> quotation is sought	for	which	N/A
39	Class of *securities quotation is sought	for	which	N/A
40			,	

Do the \*securities rank equally in all | N/A respects from the date of allotment with an existing +class of quoted +securities?

If the additional securities do not

• the date from which they do

rank equally, please state:

- the extent to which they participate for the next dividend, (in the case of a trust, distribution) or interest payment
- the extent to which they do not rank equally, other than in relation to the next dividend, distribution or interest payment
- 41 Reason for request for quotation N/A

Example: In the case of restricted securities, end of restriction period

(if issued upon conversion of another security, clearly identify that other security)

42 Number and \*class of all \*securities quoted on ASX (including the securities in clause 38)

Number	†Class	
N/A	N/A	
	1	

Appendix 3B Page 6

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

### Quotation agreement

- <sup>†</sup>Quotation of our additional \*securities is in ASX's absolute discretion. ASX may quote the \*securities on any conditions it decides.
- We warrant the following to ASX.
  - The issue of the \*securities to be quoted complies with the law and is not for an illegal purpose.
  - There is no reason why those \*securities should not be granted \*quotation.
  - An offer of the \*securities for sale within 12 months after their issue will
    not require disclosure under section 707(3) or section 1012C(6) of the
    Corporations Act.

Note: An entity may need to obtain appropriate warranties from subscribers for the securities in order to be able to give this warranty

- Section 724 or section 1016E of the Corporations Act does not apply to any applications received by us in relation to any \*securities to be quoted and that no-one has any right to return any \*securities to be quoted under sections 737, 738 or 1016F of the Corporations Act at the time that we request that the \*securities be quoted.
- We warrant that if confirmation is required under section 1017F of the Corporations Act in relation to the \*securities to be quoted, it has been provided at the time that we request that the \*securities be quoted.
- If we are a trust, we warrant that no person has the right to return the \*securities to be quoted under section 1019B of the Corporations Act at the time that we request that the \*securities be quoted.

1/1/2003

<sup>+</sup> See chapter 19 for defined terms.

- We will indemnify ASX to the fullest extent permitted by law in respect of any claim, action or expense arising from or connected with any breach of the warranties in this agreement.
- We give ASX the information and documents required by this form. If any information or document not available now, will give it to ASX before \*quotation of the \*securities begins. We acknowledge that ASX is relying on the information and documents. We warrant that they are (will be) true and complete.

Sign here:

Natalie Korchev

Date: 27 October 2004

Company secretary

Print name:

Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.

2004 NOV 15 P 12: 24 ·

OFFICE OF INTERMATIONAL CORPORATE FINANCE

Rule 4.7B

### **Appendix 4C**

### Quarterly report for entities admitted on the basis of commitments

Introduced 31/3/2000. Amended 30/9/2001

rvaine of chirty			
ANTISENSE	THERAI	PEUTICS	LIMITE

ABN

41 095 060 745

Quarter ended ("current quarter")

30 SEPTEMBER 2004

### Consolidated statement of cash flows

Cash	flows related to operating activities	Current quarter	Year to date (3 months)
1.1	Receipts from customers	\$A'000	\$A'000
1.2 1.3 1.4 1.5 1.6 1.7	Payments for (a) staff costs (b) advertising and marketing (c) research and development (d) leased assets (e) other working capital *  Dividends received Interest and other items of a similar nature received Interest and other costs of finance paid Income taxes paid Other (provide details if material) - Income Tax refund	(557) - (1,540) - (200) - 210	(557) - (1,540) - (200) - 210
	Net operating cash flows	(2,087)	(2,087)

<sup>\*</sup> Includes GST paid to suppliers and GST credits received from ATO.

<sup>+</sup> See chapter 19 for defined terms.

		Current quarter \$A'000	Year to date (3 months) \$A'000
1.8	Net operating cash flows (carried forward)	(2,087)	(2,087)
	Cash flows related to investing activities		
1.9	Payment for acquisition of:		•
	(a) businesses (item 5) (b) equity investments		-
	(c) intellectual property	-	-
	(d) physical non-current assets	(10)	(10)
	(e) other non-current assets	-	-
1.10	Proceeds from disposal of:		
	(a) businesses (item 5)	-	-
	(b) equity investments	-	-
	(c) intellectual	-	-
	property (d) physical non-	-	-
	current assets	-	-
	(e) other non-current assets	-	-
1.11	Loans to other entities	-	-
1.12	Loans repaid by other entities	-	-
1.13	Other (provide details if material)	-	-
	Net investing cash flows	(10)	(10)
1.14	Total operating and investing cash flows	(2,097)	(2,097)
1.15	Cash flows related to financing activities Proceeds from issues of shares, options, etc.	1	1
1.16	Proceeds from sale of forfeited shares		
1.17	Proceeds from borrowings		
1.18	Repayment of borrowings		
1.19	Dividends paid		
1.20	Other - costs relating to issue of shares	1	1
	Net financing cash flows	•	
	Net increase (decrease) in cash held	(2,096)	(2,096)
1.21	Cash at beginning of quarter/year to date	14,421	14,421
1.22	Exchange rate adjustments to item 1.20	- 1,132	,
1.23	Cash at end of quarter	12,325	12,325

<sup>+</sup> See chapter 19 for defined terms.

		Current quarter \$A'000	Year to date (3 months) \$A'000
1.8	Net operating cash flows (carried forward)	(2,087)	(2,087)
1.9	Cash flows related to investing activities Payment for acquisition of:  (a) businesses (item 5)	-	-
	(b) equity investments (c) intellectual property (d) physical non-current assets (e) other non-current assets	(10)	(10)
1.10	Proceeds from disposal of:		
	(a) businesses (item 5) (b) equity investments (c) intellectual property (d) physical non-current assets (e) other non-current assets	- - - - - -	-
1.11 1.12 1.13	Loans to other entities  Loans repaid by other entities  Other (provide details if material)	- - -	- - -
	Net investing cash flows	(10)	(10)
1.14	Total operating and investing cash flows	(2,097)	(2,097)
1.15	Cash flows related to financing activities Proceeds from issues of shares, options, etc.	1	1
1.16 1.17 1.18 1.19 1.20	Proceeds from sale of forfeited shares Proceeds from borrowings Repayment of borrowings Dividends paid Other - costs relating to issue of shares		
	Net financing cash flows	1	1
	Net increase (decrease) in cash held	(2,096)	(2,096)
1.21 1.22	Cash at beginning of quarter/year to date Exchange rate adjustments to item 1.20	14,421	14,421
1.23	Cash at end of quarter	12,325	12,325

<sup>+</sup> See chapter 19 for defined terms.

### Payments to directors of the entity and associates of the directors Payments to related entities of the entity and associates of the related entities

		Current quarter \$A'000
1.24	Aggregate amount of payments to the parties included in item 1.2	488
1.25	Aggregate amount of loans to the parties included in item 1.11	

	26	Explanation necessary	y for an understanding	of the transaction
--	----	-----------------------	------------------------	--------------------

Item 1.24 Reflects the following related party payments:

- (a) Total amounts paid to directors include director's fees, salaries and superannuation of \$142,214 (YTD: \$142,214).
- (b) Dr Stanley Crooke, a director of the Company is also a director of Isis Pharmaceuticals Inc ("Isis"). A total amount of \$296,799 (YTD: \$296,799) was paid to Isis for research and development related services provided by them to Antisense Therapeutics Limited ("ATL").
- (c) Professor George Werther, a director of the company, is an executive officer of the Murdoch Childrens Research Institute ("MCRI"). An amount of \$48,586 (YTD: \$48,586) was paid to the MCRI for facilities provided and services performed by them for ATL.

### Non-cash financing and investing activities

2.1	Details of financing and investing transactions which have had a material effect on consolidated
	assets and liabilities but did not involve cash flows

Not applicable.	 			

2.2	Details of outlays made by other entities to establish or increase their share in businesses in which
	the reporting entity has an interest

Not applicable.		

### Financing facilities available

Add notes as necessary for an understanding of the position. (See AASB 1026 paragraph 12.2).

		Amount available \$A'000	Amount used \$A'000
3.1	Loan facilities	-	-
3.2	Credit standby arrangements	-	-

<sup>+</sup> See chapter 19 for defined terms.

### Reconciliation of cash

show	nciliation of cash at the end of the quarter (as in the consolidated statement of cash flows) to lated items in the accounts is as follows.	Current quarter \$A'000	Previous quarter \$A'000
4.1	Cash on hand and at bank	1,825	3,921
4.2	Deposits at call	10,500	10,500
4.3	Bank overdraft	•	-
4.4	Other (provide details)	-	•
	Total: cash at end of quarter (item 1.23)	12,325	14,421

## Acquisitions and disposals of business entities

	,	Acquisitions (Item 1.9(a))	Disposals (Item 1.10(a))
5.1	Name of entity	Not applicable	Not applicable
5.2	Place of incorporation or registration		
5.3	Consideration for acquisition or disposal		
5.4	Total net assets		
5.5	Nature of business		

# Compliance statement

- 1 This statement has been prepared under accounting policies which comply with accounting standards as defined in the Corporations Act (except to the extent that information is not required because of note 2) or other standards acceptable to ASX.
- 2 This statement does give a true and fair view of the matters disclosed.

Sign here:

Natalie Korchev......

Company Secretary

Date:

27 October 2004

Print name:

Natalie Korchev

<sup>+</sup> See chapter 19 for defined terms.

# Notes

- 1. The quarterly report provides a basis for informing the market how the entity's activities have been financed for the past quarter and the effect on its cash position. An entity wanting to disclose additional information is encouraged to do so, in a note or notes attached to this report.
- 2. The definitions in, and provisions of, AASB 1026: Statement of Cash Flows apply to this report except for the paragraphs of the Standard set out below.
  - 6.2 reconciliation of cash flows arising from operating activities to operating profit or loss
  - 9.2 itemised disclosure relating to acquisitions
  - 9.4 itemised disclosure relating to disposals
  - 12.1(a) policy for classification of cash items
  - 12.3 disclosure of restrictions on use of cash
  - 13.1 comparative information
- 3. Accounting Standards. ASX will accept, for example, the use of International Accounting Standards for foreign entities. If the standards used do not address a topic, the Australian standard on that topic (if any) must be complied with.

<sup>+</sup> See chapter 19 for defined terms.

# Change to company details

- A1 Change of address
- A2 Change of name officeholders or members
- A3 Change ultimate holding company
- B1 Cease company officeholder
- B2 Appoint company officeholder
- B3 Special purpose company

- C1 Cancellation of shares
- C2 Issue of shares
- C3 Change to share structure
- C4 Changes to the register of members

Company details	Company name	
,,	ANTISCUSE THERAPEUT	ics Limites
efer to guide for information about	ACN/ABN:	Corporale key
prporate key	41 095 060 745	78841339
	i santanti peringgan peringgan penggan penggan penggan penggan penggan penggan penggan penggan penggan penggan Penggan penggan pengga	ran tunnerak pangkan kangkan kangkan pangkan kangkan kangkan pangkan pangkan pangkan pangkan pangkan pangkan b
odgement details	Who should ASIC contact if there is a query about this	form?
	Name	。""你看这样,我们也是我的是我们。""你是这样,我们就是这样。"
	MATALIE KORGIE	
	ASIC registered agent number (if applicable).	
	Telephone number	
	(03) 9827 8999	
•	Postal address	
	LEVELI, 10 would	EAUSTUE
	TOOLANC. VIC. 3	142
	Total number of pages including this cover sheet Plea	se provide an estimate of the time taken to complete this fo
	6	lus mins
	A read risk and the second read read read the control of the second read read read read read read read rea	er man felt mag en
Signature		
his form must be signed by a current	officeholder of the company.	
	. I certify that the information in this cover sheet and the atta	sched sections of this form are true and complete.
	Name	
	NATALLE FORCHEV	
	Capacity	
	Director	
	Company secretary	
	Signature	
		uest. Diktori santitit, sekudakai katalaharah akan labasa dika 1990-teknang basasa kata basar basa bahatan. Tan
	N. Korchel	
	Date signed	
,	27,10,04	
	D D M M TY YI	
	and the property of the state o	goraccions, proprietas per este de cen en e
Lodgement	Send completed and signed forms to:	For help or more information
	Australian Securities and Investments Commission,	Telephone 03 5177 3988
	PO Box 4000, Gippsland Mail Centre VIC 3841.	Email info.enquiries@asic.gov.au

Or lodge the form electronically by visiting the ASIC website

www.asic.gov.au

Web

www.asic.gov.au

# Section C completion guide

### Standard share codes

Refer to the following table for the share class codes for sections C1, C2, C3 and C4

Share class	code Full title	Share class of	code Full (itte
A	A	PRF	preference
В	Betc	CUMP	cumulative preference
EMP	employee's	NCP	non-cumulative preference
FOU	founder's	REDP	redeemable preference
LG	life governor's	NRP	non-redeemable preference
MAN	management.	CRP	cumulative redeemable preference
ORD	ordinary	NCRP	unu Pulita un aktionata Pilita, Raud kai este profilir l'application Pitter Pilit et Raul es cui vi escribir u d
RED	redeemable	PARP	non-cumulative redeemable preference participative preference
SPE	special		participative preference
if you are usi	ng the standard share class o	odes vou do not pood to	provide the full title for the shares, just the share class
code:		ooo jou do not need to	provide the full title for the shares, just the share class.

If you are not using the standard share class code, enter a code of no more than 4 letters and then show the full title

## Sections to complete

Use the table below to identify the sections of this form to complete (please indicate the sections that have been completed). Completion of this table is optional.

	C1 - Cancellation of shares	C2 - Issue of shares	C3 - Change to share structure table	C4 - Change to members register
Issue of shares				
Propnetary company.	Not required		1	
Public company (7)				<b>/</b>
fin response to the Annual company statement	Not required		V	Z
if not in response to the Annual company statement.	Not required		A LANGUAGE CONTRACTOR OF THE PROPERTY OF THE P	
Cancellation of shares			Not required	Not required
Proprietary company		Not required:		
Public company Public company		i i i i i i i i i i i i i i i i i i i	<b>V</b>	1
if in response to the Annual		Not required		
Company statement				1
if not in response to the Annual company statement	<b>V</b>	Not required	Not required	Not required.
Transfer of shares				
Proprietary company	Not required	Not required	Not required	<b>7</b>
Public company:  If in response to the Annual				1
company statement	Not required	Not required:	Not required	1
If not in response to the Annual company statement	Not required	Not required	Not required	Not required
Changes to amounts paid				
Proprietary company	Not required	Not required		Z
Public company				
if in response to the Annual company statement	Not required	Not required		
if not in response to the Annual company statement	Not required:	Not required		
Changes to beneficial ownership.			Not required	Not required
Proprietary company	Not required	Not required		
Public company			Not required:	
if in response to the Annual	Not required	Not required		
company statement			Not required	<b>Y</b>
If not in response to the Annual company statement	Not required	Not required	Not required	Not required

To notify ASIC about a division or conversion of a class of shares, you must lodge a form 211 within 28 days of the change occurring.

To notify ASIC about a conversion of shares into larger or smaller numbers, you must lodge a form 2205B within 28 days of the change occurring.

Reason for cancellation	Redeemable preference shares — \$.254J						
Please indicate the reason that shares have been cancelled (select one or more	Redeemed out of profits						
poxes)	Redeemed out of proceeds of a fresh issue of shares						
## ### ### ### ### ### ### ### ### ###	Capital reduction — S:256A – S:256E						
	Single:shareholder company  Multiple shareholder company. A Form 2560 must be lodged before a capital reduction takes place.						
	Share buy-backss:257H(3):						
\$45 \$15 \$25 \$25 \$25 \$25 \$25 \$25 \$25 \$25 \$25 \$2	Minimum holding buy-back by listed company						
	Other buy-back type. A form 280 or 281 must be lodged at least 14 days, and no more share buy-back can take place	than'i year before th					
	Forfeited shares — S.258D						
M M M M M M M M M M M M M M M M M M M	Shares returned to a public company—ss.258E(2) & (3)						
	Undersection 651C, 724(2), 737 or 738						
	Under section:1325A (court order)						
	Oher,						
	Description						
) (1) (1) (1) (1) (1) (1) (1) (1) (1) (1	Give section reference:						
\$5.5 \$1.5 \$2.5 \$2.5 \$2.5							
Details of cancelled shares	List the details of shares cancelled in the following table: Share:class code::::Number.of shares cancelled::::Amount paid (cash or otherwise):::						
	Share: class code Number of shares cancelled. Amount paid (cash or otherwise)						
		1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1					
		THE STATE OF THE S					
	Earliest date of change						
72 72 72 72 72 72 72 72 72 72 72 72 72 7	Please indicate; the earliest date that any of the above changes occurred.						
***	D D M M T Y						

are class code	Number of shares issued	Amount paid per	share	Amount unpaid per shar	re.
ord	140	20	CSUS	NIL	
-					
					<del></del>
lest date of chan	ge inlest date that any of the above chan	ges occurred			
4,10	104			775 100 100 100 100 100 100 100 100 100 10	
. D] . [M . M]	ties of Targeties of Artista President Color and and afficient at the state and are the color of		willen contract?		
ares were issued	tor other than cash, were some or all.				Such dudenka hiderami birkin
ares were issued Yes	for other than cash, were some or all				
Yes if yes, proprieta	ary companies: must also lodge a For			blic companies must also	lodge a Form 2
Yes if yes, propriets and either a Fo				blic companies must also	lodge a Form 2
Yes If yes, propoet and either a Fo	ary companies: must also lodge a For	m 207Z certifying that all stam	p duties have been paid. Pu		
Yes flyes prophet and either a Fo No if no; propheta	ary companies: must also lodge a For orm 208 or a copy of the contract ry companies are not required to prov	m 207Z certifying that all stam	p duties have been paid. Pu		
Yes If yes, propriet and either a Fo No If no, proprieta  Change to	ary companies; must also lodge a For orm 208 or a copy of the contract; ry companies are not required to prov o share structure	m 207Z certifying that all stam	p duties have been paid: Pu	s must also lodge a Form	208
Yes If yes, proposel, and either a Fo No If no, proprieta  Change to the a change to the	ary companies: must also lodge a For orm 208 or a copy of the contract ry companies are not required to prov	m 207Z certifying that all stam ide any further documents with	p duties have been paid: Pu	s must also lodge a Form	208
Yes flyes, prophete and either a Fo No if no, propheta  Change to e a change to the ed. Details of share	ary companies: must also lodge a For orm 208 or a copy of the contract:  ry companies are not required to prove share structure share structure table has occurred (eg	m 207Z certifying that all stam ide any further documents with	p duties have been paid. Puntis form: Public companie  ncellation of shares), please	s must also lodge a Form e show the updated details Total amount.	208 s for the share cl
Yes flyes, prophete and either a Fo No if no, propheta  Change to e a change to the ed. Details of share	ary companies; must also lodge a For orm:208 or a copy of the contract; ry companies are not required to prove share structure share structure table has occurred (equire classes not affected by the change	m 207Z certifying that all stam ide any further documents with	p duties have been paid. Pu n this form: Public companie ncellation of shares), please	e show the updated details  Total amount paid on these	2083 s for the share cl
fyes, proprieta and either a Fo	ary companies; must also lodge a For orm 208 or a copy of the contract; or companies are not required to prove share structure table has occurred (expectasses not affected by the change Full title if not standard.	m 207Z certifying that all stam ide any further documents with	p duties have been paid: Punths form: Public companie  ncellation of shares), please  lotal number of shares (current after changes)	s must also lodge a Form e show the updated details Total amount paid on these shares	s for the share cl Total amount urpaid on these shares
fyes, proprieta and either a Fo No If no, proprieta  Change to e a change to the ed. Details of share	ary companies; must also lodge a For orm 208 or a copy of the contract; or companies are not required to prove share structure table has occurred (expectasses not affected by the change Full title if not standard.	m 207Z certifying that all stam ide any further documents with	p duties have been paid: Punths form: Public companie  ncellation of shares), please  lotal number of shares (current after changes)	s must also lodge a Form e show the updated details Total amount paid on these shares	s for the share cl Total amount urpaid on these shares
fyes propriets and either a Fo	ary companies; must also lodge a For orm 208 or a copy of the contract; or companies are not required to prove share structure table has occurred (expectasses not affected by the change Full title if not standard.	m 207Z certifying that all stam ide any further documents with	p duties have been paid: Punths form: Public companie  ncellation of shares), please  lotal number of shares (current after changes)	s must also lodge a Form e show the updated details Total amount paid on these shares	i208. If or the share class of the share class on these shares.
fyes propriets and either a Fo	ary companies; must also lodge a For orm 208 or a copy of the contract; or companies are not required to prove share structure table has occurred (expectasses not affected by the change Full title if not standard.	m 207Z certifying that all stam ide any further documents with	p duties have been paid: Punths form: Public companie  ncellation of shares), please  lotal number of shares (current after changes)	s must also lodge a Form e show the updated details Total amount paid on these shares	i208. If or the share class of the share class on these shares.
fyes propriets and either a Fo	ary companies; must also lodge a For orm 208 or a copy of the contract; or companies are not required to prove share structure table has occurred (expectasses not affected by the change Full title if not standard.	m 207Z certifying that all stam ide any further documents with	p duties have been paid: Punths form: Public companie  ncellation of shares), please  lotal number of shares (current after changes)	s must also lodge a Form e show the updated details Total amount paid on these shares	i208. If or the share class of the share class on these shares.

Is this document being lodged to update the Annual Company Statement that was sent to you?

ASIC Form 484

Lodgement details

Yes

# C4 Changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

e changes apply to ease indicate the name and address the member whose shareholding has			y name	,	iven names		lengther in the property of the	1
member whose ged	e snarenoiding nas	-OR						
		Comp	pany name					
		ACN/ARBN	V ABN					
		Office unit	level, or PO Box	number	**************************************	Process and		
		Street num	ber and Street na	me				
		Suburb/Cit	<b>y</b>				naiceo I	emtory
							State/I	emory
		Postcode	ing samples Samples	Country (if no	(Australia)			
est date of chase indicate the control of the following char	earliest date that a	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	ange / \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	∖ Y				
	- A - F - A - C - C - C - C - C - C - C - C - C		took have took to a been been been and to be	241-14-170-2 (V. 1924, AVIII)	2.02.07.04.22.04.22.04.000.000.000.000.000.000.	*** 6.24 14 17 14 15 14 18 15 15 15 1	Tartes   1. (2.192)   1. (2.29 )   1. (2.19 )	A PROPERTY OF THE PROPERTY OF
Share class	Shares increased by (number)	Shares decreased by (number)	Total number now held	Total \$ paid on these shares	Total \$: unpaid on these	Fully paid: (y/n).	Beneficially held (y/n)	Top 20 member (y/n)
hare class	Shares increased by	decreased by		on these	unpaid			
hare class	Shares increased by	decreased by		on these	unpaid on these			
Share class	Shares increased by	decreased by		on these	unpaid on these			
Share class	Shares increased by (number)	decreased by (number)	now held	on these	unpaid on these			
	Shares increased by	decreased by (number).	now held	on these	unpaid on these			

ASIC Form 484 26 February 2004 Section C Page 4 of 5

# C4 Continued... Further changes to the register of members

Use this section to notify changes to the register of members for your company (changes to the shareholdings of members):

- If there are 20 members or less in a share class, all changes need to be notified
- If there are more than 20 members in a share class, only changes to the top twenty need be notified (s178B)
- If shares are jointly owned, you must also provide names and addresses of all joint owners on a separate sheet (annexure), clearly indicating the share class and with whom the shares are jointly owned

e changes apply to ase indicate the name and address he member whose shareholding has		Famil	/name	Leavent paint	iven names	and the state of t			
ged	o differentially flag	OR Comp	any name						
		ACN/ARBN	(ABN						
		777	level, or PO Box per and Street na						
		Suburb/City	THE STANK AND PRESENT SHEAR WATER				l State/	iemtory	
		Postcode							
liest date of chase indicate the	earliest date that any		Date of change  Discontinuous programmes and the continuous progra						
he changes are Share class code	Shares	Shares: decreased by (number)	Total number now held:	"Total \$ paid on these shares	Total \$ unpaid on these	Fully paid (y/n)	Beneficially held (y/n)	Top:20 member (y/n)	
Valentaria)					shares				
* Public compan	ies are not required to p	ovide these deta	is (Control of the Control of the Co						
	nember's name in	Date of e	7. Prepar (2004. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 1920. 192						

# ANTISENSE THERAPEUTICS

2 September 2003

The Companies Section
The Australian Stock Exchange Limited
530 Collins Street
MELBOURNE VIC 3000

Dear Sir/Madam



Dear Shareholder

I am pleased to advise you that the directors of Antisense Therapeutics Limited ('Antisense') have established a share purchase plan ('Plan') to give existing shareholders the opportunity to purchase additional shares in Antisense.

Under the Plan your directors are offering shareholders the opportunity to purchase a maximum of \$5,000 worth of Antisense shares. Shares purchased under the Plan will not attract brokerage, stamp duty or any other transaction costs.

As you may be aware, Antisense recently raised additional capital of \$5 million for its drug development projects (including ATL1102 for multiple sclerosis and ATL1101 for psoriasis) by way of a private placement to 'exempt' professional investors. The Plan provides Antisense's other loyal investors with the opportunity to also participate in Antisense's equity raising programs without incurring any charges.

An offer is being made under the Plan to all shareholders, whose registered address is in Australia, who owned ordinary shares in Antisense at close of trade on 1 September 2003 including those shareholders who had purchased ordinary shares in Antisense in accordance with ASX Listing Rules by no later than the close of trade on that day. The offer is non-renounceable, which means that you cannot transfer your right to purchase shares under the offer to anyone else. Details of the offer are set out in the Offer and Acceptance Form and Terms and Conditions attached.

Applications must be made for a minimum of \$1,000 worth of shares, with multiples thereafter of \$1,000, up to a maximum of \$5,000 worth of shares. The shares will be issued at 13 cents per share which is the issue price paid by Australian institutions and professional investors in the Company's recent share placement.

The offer under the Plan has been structured to comply with ASIC Class Order 02/831. As such, the maximum application for \$5,000 worth of shares applies to all eligible shareholders even if they receive more than one offer from Antisense (for example, because they are a

joint holder of shares or because they hold more than one shareholding under separate share accounts). Antisense reserves the right to reject any application for shares where it believes this requirement has not been complied with.

The offer closes at 5.00 pm AEST on 1 October 2003 ('Closing Date'). To participate in the offer, you will need to return your completed Offer and Acceptance Form together with your cheque in Australian dollars for the full amount to which your acceptance relates so that it is received by Computershare Investor Services Pty Ltd (as detailed in the Offer and Acceptance Form) no later than 5.00 pm AEST on the Closing Date. Applications received after the Closing Date will not be accepted.

It is expected that shares issued under the Plan will be quoted on Australian Stock Exchange on or about 13 October 2003 and you should receive your holding statement shortly after this date.

In deciding whether to take up the enclosed offer of shares, you should seek your own independent financial, legal and taxation advice in respect of the offer.

If you have any questions in relation to the Plan, please contact the Company's share registry, Computershare Investor Services Pty Limited on 1300 850 505 or + 61 3 9615 5970.

Yours sincerely

Robert Moses Chairman

Antisense Therapeutics Limited

SHARE PURCHASE PLAN ("PLAN") GPO Box 52 Melbourne, Victoria 8060 APPLICATION FORM Enquiries (within Australia) 1300 850 505 (outside Australia) 61 3 9615 5970 Facsimile 61 3 9473 2529 web.queries@computershare.com.au www.computershare.com Record Date: 4 September 2003 Shareholder Name & Address: Opening Date: 10 September 2003 Closing Date: 1 October 2003 Issue Date: 8 October 2003 BAR CODE 100000000000 A APPLICATION I/We, the above shareholder(s), being registered as ordinary shareholder(s) in the Company as at the Record Date for this offer do hereby apply for new shares as indicated below at an issue price calculated in accordance with the Terms and Conditions of the Antisense Therapeutics Limited Share Purchase Plan, as attached and as otherwise set out in the accompanying letter dated 5 September 2003. Applications must be made for a minimum of \$1,000 worth of shares, with multiples of \$1,000 thereafter, up to a maximum of \$5,000 worth of shares. Please tick the appropriate box \$5,000 \$2,000 \$3,000 \$4,000 \$1,000 B PAYMENT DETAILS " INSERT DETAILS OF YOUR CHEQUE OR BANK CHEQUE - PLEASE COMPLETE IN BLOCK LETTERS Drawer **BSB** Amount A\$

c/- Computershare Investor Services Pty Ltd

## C CERTIFICATION

ABN 41 095 060 945

For the purpose of the ASIC Class Order 02/831, you certify and confirm that the aggregate price for:

- (a) shares you have applied for under this application; and
- (b) any other shares you have applied for under this Plan or any other Company share purchase plan or similar arrangement in the 12 months prior to the date of your application, (including through joint and/or beneficial holdings) does not exceed \$5,000.

Signature(s): \_\_\_\_\_\_ Date: \_\_\_\_\_

- 1. If you want to participate in this offer, please carefully read the Terms and Conditions of the offer attached.
- 2. Complete all the required details on the Application Form, noting that all amounts are expressed in Australian Dollars.
- 3. Write the cheque for the exact amount of the Shares you want to acquire. Please make the cheque payable to Antisense Therapeutics Limited.
- Please return the Application Form, together with the cheque, to Computershare Investor Services Pty Limited, GPO Box 52, Melbourne, Victoria 8060.
- Ensure that your Application Form and cheque reach us by the closing date of the offer being no later than AEST 5 pm on 1
  October 2003.
- 6. If signed under power of attorney, the attorney states that they have not received a notice of revocation of that power.

By accepting this offer you agree to be bound by the Terms and Conditions of the Offer and the Constitution of the Company.

# ANTISENSE THERAPEUTICS LIMITED SHARE PURCHASE PLAN

Pursuant to the Antisense Therapeutics Limited Share Purchase Plan ("Plan"), Antisense Therapeutics Limited ABN 41 095 060 745 ("Antisense") offers eligible shareholders the ability to apply for a minimum of \$1,000 and a maximum of \$5,000 worth of fully paid ordinary shares ("Shares") in Antisense ("Offer").

If you are eligible to apply for Shares, you may apply for a minimum of \$1,000 worth of Shares and in multiples of \$1,000 thereafter, up to a maximum of \$5,000 worth of Shares.

Please carefully read the Terms and Conditions relating to the Offer as you will be bound by them. By lodging this form with your cheque, you confirm that you have read, understood and agreed to the terms and conditions of the Plan.

#### TERMS AND CONDITIONS

#### 1. Participation

Participation in the Plan is open to all persons who, as at the record date determined by the directors of Antisense ('Board'), are registered as holders of ordinary shares in Antisense, except those shareholders whose registered address is in a country where, in the reasonable opinion of the Board, it is unlawful or impractical for Antisense to issue offers under the Plan.

Participation in the Plan is optional and is subject to these terms and conditions.

#### 2. Offers

Offers under the Plan will be non-renounceable and shares may be issued only to the shareholder to whom they are offered

Each offer will be made on the same terms and conditions. All eligible shareholders of Antisense will receive the same offer, irrespective of the number of shares which they hold on the record date.

Offers to subscribe for shares under the Plan may be made once a year, or as otherwise determined by the Board. In any consecutive 12 month period, the maximum value of shares for which each eligible shareholder may subscribe under the Plan is \$5,000 (or such lesser amount as the Board may determine in its discretion). This limit applies to each shareholder even if that person holds shares in more than one capacity – for example, as a sole holder and as a first (or subsequent) named holder of two or more joint holders. However, a trustee or nominee expressly noted on a company register may receive an offer for each occasion they are separately recorded as a trustee or nominee for a different beneficiary named on that register.

Offers will be made subject to any terms and conditions that the Board thinks fit which are consistent with these terms and conditions, including any minimum subscription amount. The Board may also determine the multiple(s) of shares, or the fixed dollar amount(s), for which each eligible shareholder may subscribe under any given offer under the Plan.

#### 3. Issue Price

Shares will be issued under the Plan at the issue price determined by the Board, which must be less than the market price during a specified period in the 30 days prior to either the date of the offer or the date of issue of shares under the offer.

#### 4. Costs of Participation

No brokerage, commissions, stamp duty or other transaction costs will be payable by shareholders in respect of the application for, and issue of, shares under the Plan.

### 5. Issue of Shares

Antisense will issue shares for the purposes of an offer as soon as reasonably practicable after the closing date of the relevant offer.

Shares issued under the Plan will rank equally with all other ordinary shares in Antisense on issue as of the date of issue and will therefore carry the same voting rights, dividend rights and other entitlements as those shares.

Antisense will apply for shares issued under the Plan to be quoted on Australian Stock Exchange Limited ('ASX').

Antisense will, within the period required by the ASX Listing Rules, send participants a holding statement in respect of any shares issued to them under the Plan.

#### 6. Acceptance of Offers

An offer to participate in the Plan may be accepted by an eligible shareholder only by completing and returning the acceptance form provided by Antisense, together with the appropriate payment for the amount to which the acceptance relates, by no later than the closing date for the offer specified on the acceptance form.

Payment may be made only by cheque in Australian dollars drawn on an Australian bank.

An offer will be taken to have been accepted by an eligible shareholder only if the cheque which accompanies the shareholder's acceptance form is paid in full on first presentation.

If one or more acceptance forms are received by an eligible shareholder in relation to shares with a value greater than \$5,000 in any consecutive 12 month period, the shareholder will be issued with the maximum number of shares permitted by the Plan and the excess subscription monies will be refunded (without interest).

If an eligible shareholder subscribes for an amount which is not exactly divisible by the issue price for the shares, in calculating the number of shares to be issued, all fractional entitlements will be rounded up to the nearest whole number.

### 7. Amendment, Suspension and Termination of the Plan

The Board may, in its discretion, amend, suspend or terminate the Plan at any time and adopt any administrative procedures it thinks appropriate in relation to the Plan. Antisense may issue to any person fewer shares than subscribed for under the Plan (or none at all) if Antisense believes that the issue and allotment of those shares would contravene any law or the rules of any stock exchange on which Antisense shares are quoted.

#### 8. Dispute Resolution

Antisense may settle, in any manner it thinks fit, any difficulties, anomalies or disputes which may arise under or in connection with the operation of the Plan, whether generally or in relation to any participant or class of participants, offer, application or shares, and the decision of Antisense shall be conclusive and binding on all participants and other persons to whom the determination relates.

Antisense reserves the right to waive compliance with any provision of these terms and conditions.

#### 9. Notices

Notices and statements to participating shareholders may be given in any manner determined by the Board from time to time.

#### 10. Privacy

Chapter 2C of the *Corporations Act 2001* requires information about shareholders (including name, address and details of the shares held) to be included in Antisense's public register. If a shareholder ceases to be a shareholder, Chapter 2C of the *Corporations Act 2001* requires this information to be retained in Antisense's public register. These statutory obligations are not altered by the *Privacy Act 1988 (Cth)* as amended. Information is collected to administer shareholders' security holdings.